FIBRO-OSSEOUS LESIONS AFFECTING THE JAWS

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DECLARATION

I, **David Stanislaw MacDonald** declare that

a. the thesis has been composed by myself, and

b. the work is my own, and

c, that the work has not been submitted for any other degree or professional qualification.

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ABSTRACT

Introduction: Fibro-osseous lesions (FOLs) affecting the jaws represent an important category both diagnostically and therapeutically. Although they share the similar histopathology, they differ with regards to their behaviour. The overwhelming majority of cases of cemento-osseous dysplasia (COD) require no treatment, whereas its florid (affects more than one sextants of the jaw) form, in particular, raises significant risks of prosthodontic failure in the elder patient. The cemento-ossifying fibroma (COF) is a benign, occasionally aggressive, neoplasm requiring complete enucleation to obviate recurrence. Fibrous dysplasia (FD) is a hamartoma in most cases, but on occasion displays neoplastic behaviour. Diagnosis is normally achieved upon both clinical and radiological evaluation. The main radiological criterion is that the margins of FD of the face and jaws are poorly defined. Still the variant behaviour of a few lesions, even after appropriate treatment, compels a better understanding of these lesions with particular regard to their manifestations in various major world populations.

Aims: 1. Review the consecutive cases of these lesions affecting a Hong Kong population, almost exclusively Chinese, whose oral lesions until only recently have not featured prominently in the international literature. 2. Conduct a systematic review (SR) on the world literature pertaining to FOLs.

Materials and Methods: All consecutive cases on CODs, COFs and FDs managed at the Dental School of the University of Hong Kong (HKU) from 1982 to 1992 for CODs and onwards to 2004 for COFs and FDs were identified; their notes, radiographs and histopathological reports on all cases were reviewed. The relevant literature was identified by electronic database, handsearching and reference list harvesting.

Results: Twenty-three Florid CODs, 6 Focal CODs, 24 COFs and 21 FDs (1 bimaxillary) were identified and their clinical and radiological features analysed and inserted into the SRs. All Florid and Focal CODs and COFs were female. Florid CODs identified as incidental findings and retained in radiology files were significantly younger than those derived from pathology files. COFs in the SR had significant predilections for females and the mandible and to be detected as radiolucencies, whereas the FD more significantly displayed radiologically, expansion of the buccolingual cortices, and of the lower border of the mandible. Clinically the Florid CODs were significantly associated with pain, FDs were more significantly associated with swelling, FocCODs were also more significantly found incidentally.

Discussion: Hitherto, Florid CODs were considered to be largely exclusive to women of African origin. Both reports from which the Florid COD material was derived helped to alert the presence of this lesion in the Chinese, who form nearly a quarter of the global population. The earlier published report on FDs was the first application of SR to the clinical and radiological presentation of a lesion affecting the face and jaws. This report and others on the other two FOLs has been revised to include reports in other world languages. Nevertheless, the detail of reporting of these lesions is still inadequate, particularly with regards to follow-up. Although the number of recurrences in both the FD and COF SRs is small, when weighted to the small number of reports that record follow-up, the recurrence rates at 8% and 6% respectively indicate that these lesions require long-term follow-up.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF MAPS

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Chapter 1.

Introduction: FIBRO-OSSEOUS LESIONS OF THE JAWS

Preamble:

In dentistry, it is firmly established that 'fibrous dysplasia' (FD) and 'cemento-ossifying fibroma' (COF) affecting the jaws, although displaying a similar range of histopathological presentations, are separate lesions differing in behaviour and presentation. They are distinguished by their radiologically determined margins. Although this view has not been so widely understood in medicine, the present author's review (MacDonald-Jankowski, 2004a) published in a medical radiology journal, *Clinical Radiology*, had disseminated it within this medical community; this review was the third most downloaded *Clinical Radiology* (Royal College of Radiologists) publication for 2004 until 2006. In addition, the 'Odontogenic tumours' section of the World Health Organisation's 2005 "Pathology and genetics of head and neck tumours", has reconfirmed this view (Slootweg and El Mofty (2005) for COF and Jundt (2005) for FD). Reichart and Philipsen, two of the 'odontogenic tumors' section editors of the above WHO document, had already cited 5 of the present author's publications in their 2004 text 'Odontogenic tumors and allied lesions'; two were of 'fibro-osseous lesions' (FOLs); FD (MacDonald-Jankowski, 1999a) and COF (MacDonald-Jankowski, 1998). In addition to FD and COF, 'cemento-osseous dysplasia' (COD), the third FOL affecting the jaws, is a recognized phenomenon within certain communities. The challenge of determining the characteristics of FOLs (if they exist), with regards to their future conduct,

remains largely unmet. Such conduct covers recurrence (following surgery, particularly of FD, but also of COF), reactivation provoked by life events such as pregnancy and menopause, and the response to restorative treatment, particularly to osseointegrated implants. It is with regard to the last that the COD can no longer be considered to be a trivial lesion; it is prevalent in certain world communities and furthermore, is already presenting clinicians with prosthodontic challenges. Although these questions are outside the scope of this thesis, the better understanding of clinico-radiological and global presentations of this and the other FOLs that this thesis addresses may form a firm basis upon which further work of such clinical import can be based.

Following confirmation that the lesion displays the range of histopathological features typical of an FOL, the definitive diagnosis of a particular FOL is made on the clinical and but more particularly the conventional radiological features. MacDonald-Jankowski and co-authors (2004b) show that advanced imaging, such as CT, has only a secondary role in diagnosis. CT only really helps, in planning treatment, to determine the extent and anatomical involvement of the already diagnosed lesion, particularly with regard to the anatomically complex maxilla. Therefore, advanced imaging is outside the scope of this thesis.

Introduction:

"The term fibro-osseous lesion is a generic designation of a group of jaw disorders" (Koury et al., 1995), characterised by the replacement of bone by a benign

connective tissue matrix. This matrix displays varying degrees of mineralisation in the form of woven bone or of cementum-like round acellular intensely basophilic structures. The last are indistinguishable from 'cementicles' (Kramer et al., 1993). Nevertheless, Summerlin and Tomich (1994) urge, "From the purist point of view the term 'cementum' should be used only for the mineralised product on the radicular portion of a tooth." They chose to refer to it as 'cementum-like' a term already used by Kramer and co-authors (1993).

The term FOL as it is used in a maxillofacial context considers lesions that differ (with the exception of FD) from those found in the rest of the skeleton (O'Hara, 1997; Unni, 1996). The term FOL in the maxillofacial region is applied to the aforementioned COD, FD and COF (Waldron, 1993) and their subtypes.

The importance of radiology to the diagnosis of FOL

Maxillofacial FOLs are of particular interest to the radiologist because they represent the central role of the radiologist in the diagnostic process. This role arises because the histopathological spectrum for all FOLs displays a similar range of presentations although they range widely in behaviour, from dysplasia, hamartoma to benign neoplasia with occasional recurrence (Slootweg and El Mofty. 2005; Jundt, 2005a) and Slootweg, 2005). The late Charles Waldron wrote "In absence of good clinical and radiologic information a pathologist can only state that a given biopsy is consistent with a FOL. With adequate clinical and radiologic information most lesions can be assigned with reasonable certainty into one of several categories"

(Waldron, 1993). Conversely in the absence of such information Eisenberg and Eisenbud (1997) stated "pathologists today will often rightly decline to render a definitive diagnosis ... Instead, the pathologist will resort to the noncommittal designation of *benign fibro-osseous lesions* [their italics]. This is the only acceptable approach considering the potential for inappropriate treatment otherwise." Therefore the identification or clarification of the majority of FOLs is made upon clinical and radiological features.

Radiological assessment of the anatomical location of a bone tumour, its shape and size, the pattern of its matrix and its destruction, the definition of its margins and concomitant soft-tissue abnormalities generally correlate with its behaviour (aggressive or benign) (Kilpatrick and Ward, 1999). 'Periosteal reaction', an important feature considered by skeletal radiologists, "is not a feature of benign fibro-osseous lesions" (Wenig et al., 1998).

Many FOLs, particularly COD (Waldron, 1993), are symptomless and require no surgery. Therefore diagnosis of the lesions on clinical and radiological features alone may obviate the need for an otherwise unnecessary invasive procedure such as biopsy. Although definitive diagnosis of the lesion as an FOL must be made on its histopathology, avoidance of surgery could benefit the patient, because exaggerated growth of FD has been stimulated by surgery in young patients (White and Pharoah, 2004).

Figure 1

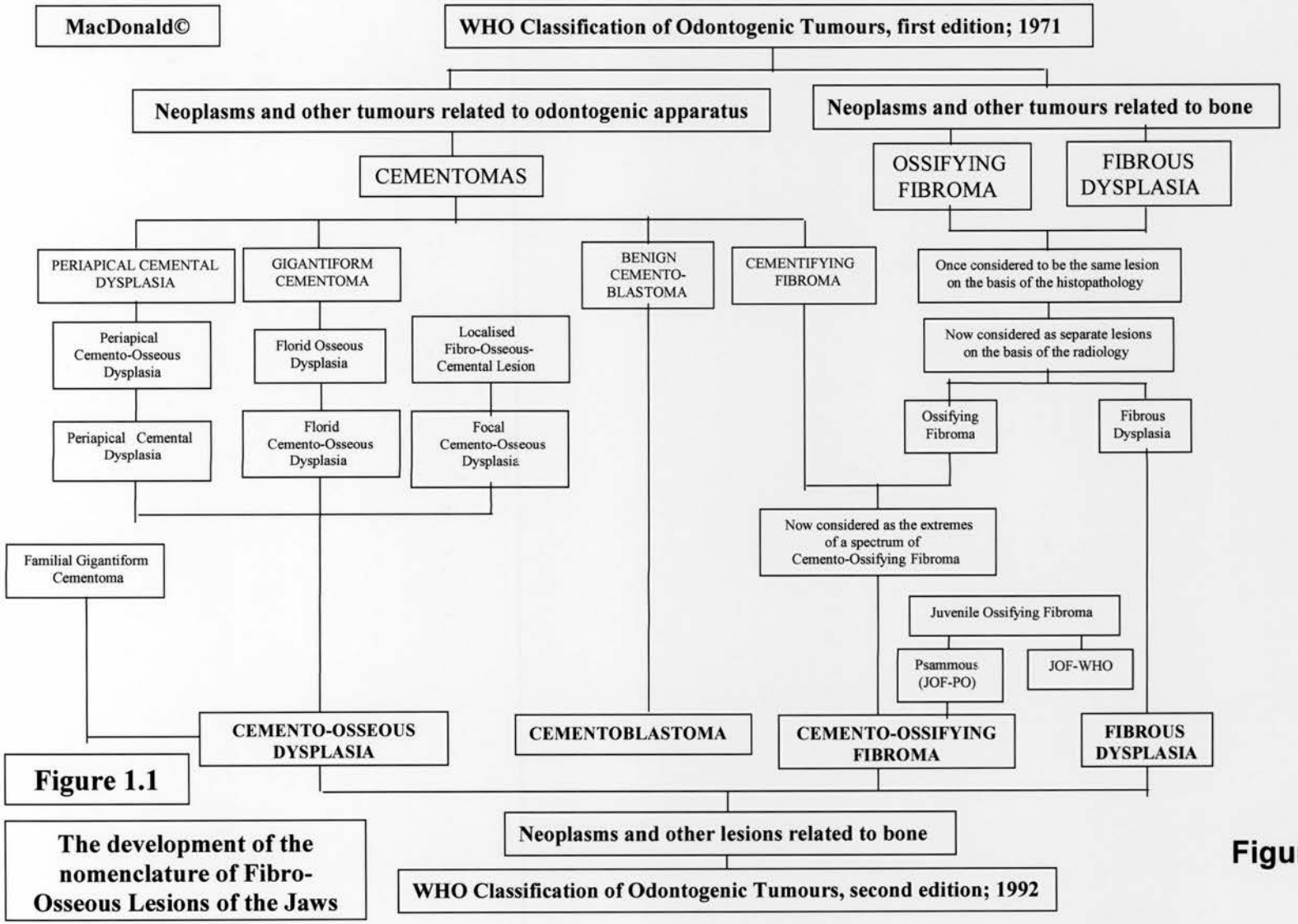


Figure 1.1

The development of the nomenclature of Fibro-Osseous Lesions of the Jaws

Figure 1.

The classification and nomenclature of FOLs

FOLs of the jaws have been subject to frequent renaming and reclassification; the development of this nomenclature and classification is summarised on Figure 1. This figure includes only those terms which appear to be still in use and therefore still clinically relevant. Nevertheless, this simplified figure is still able to display the 'lumping' and 'splitting' that appear to attend frequently the development of most classifications and systems of nomenclature. In the first edition of the WHO Classification of `Odontogenic Tumours' (1971) four lesions, containing cementum-like structures, were identified (Pindborg et al., 1971). [The history of this classification has been recently reviewed by Philipsen and Reichart (2006).] These 'cementomas' were the 'benign cementoblastoma' and the 'cementifying fibroma', 'periapical cemental dysplasia' and the 'gigantiform cementoma'. They were placed within the 'neoplasms and other tumours related to odontogenic apparatus' category. FD and 'ossifying fibroma', the other lesions that are frequently histologically indistinguishable, were placed in the category of 'neoplasms and other tumours related to bone'. Since then a number of amendments to this classification had become necessary. The observation of identical cementum-like tissue in lesions in extragnathic sites suggested that this tissue may be a merely normal variant of bone (Friedman and Goldman, 1967); and that dental cementum itself is a specialised form of 'bundle-bone' (Kramer et al., 1992). Therefore, in the second edition of the WHO's classification in 1992 (Kramer et al., 1992), three of the 'cemental' lesions were transferred to the 'neoplasms and other tumours related to bone' group, leaving the benign cementoblastoma as the sole true neoplasm of dental cementum. A

number of recent medical texts still refer to the first edition, such as that by Unni (1996).

Although the term FOL is not mentioned by the authors of WHO's second edition (Kramer et al., 1992), their broad re-classification of these lesions based both on behaviour and histopathology is entirely consistent with Waldron's recommendations (Waldron, 1985). The FOLs can now be considered to be a subset of 'Neoplasms and other tumours related to bone'.

The radiology of FOLs affecting the face and jaws

Fibrous Dysplasia

FD is an important lesion affecting the maxillofacial region because it can cause severe deformity and asymmetry, and, most devastating of all, blindness. "FD is a genetically-based sporadic disease of the bone"; its "Mutations in the gene (GNAS I) encoding for the α-subunit of a signal transducing G-protein (Gs-α) lead to increased c-AMP production affecting proliferation and differentiation of preosteoblasts" (Jundt, 2005a). Bianco and co-authors (1998) have been able to reproduce human FD in mice by transplanting mosaics of normal and Gs-α progenetic cells. Successful transplantation requires both the normal and abnormal cells. This and the range of FD's behaviour suggest that the pathenogenesis of FD may be complex. Chapurlat and Meunier (2000) have proposed recently such a pathenogenesis which interrelates many of the salient features, elevated cAMP,

increased expression of the proto-oncogene, c-fos, abnormally differentiated osteoblasts, formation of abnormal bone, increase in sex steroid receptors, increased interleukin-6 (target of diphosphanate treatment) and osteoclasts. Furthermore, the classical division of FD into monostotic, polyostotic and McCune-Albright forms may reflect the timing of the mutation and thereby the initial size of the mass of FD precursor cells (Cohen and Howell, 1999). The polyostotic form occurs in childhood whereas the monostotic may occur postnatally. This correlates with the evidence that the monostotic form is not a precursor of the polyostotic form (Lustig et al., 2001).

The monostotic form accounts for 80 to 85% of cases of FD. Three percent of the polyostotic form have endocrinopathies (Waldron, 1993) and are cases of McCune-Albright syndrome (precocious puberty and café-au-lait spots). McCune-Albright syndrome will not be considered further, because Fahmy and co-authors (2000) have already fully discussed the radiology of precocious puberty and its extensive differential diagnosis. Polyostotic FD, especially when bilateral, can appear as part of 'Mazabraud syndrome', which features intramuscular myxomas (Faivre et al., 2001); there does not appear to be a reported case specifically affecting the jaws. Riminucci and co-authors (2001) refined further the FD genotype further, distinguishing McCune-Albright syndrome from gnathodiaphyseal dysplasia (which affects the jaws and causes bowing and sclerosis of tubular bones). Although the term 'monostotic' can be readily applied to cases of FD affecting the mandible alone, this may not be so for FD affecting the maxilla. There, FD can affect contiguous bones such as the zygoma. These cases have been called 'craniofacial FD' (Waldron, 1993).

Polyostotic and McCune-Albright forms are easily diagnosed on clinical and radiological investigation alone. A radiological regime for polyostotic FD used by medical radiologists is scintigraphy and then plain film radiography of areas of increased radiolabelled uptake or activity. This is not so with the monostotic form which has a number of other important lesions in its differential diagnosis requiring bone biopsy. Bone biopsy is generally avoided particularly where the risk of pathological fracture is high (Chapurlat and Meunier, 2000). FD of the mandible differs in another important aspect from FD affecting long bones in that there does not appear to have been an unequivocal report of pathological fracture of a dysplastic mandible (MacDonald-Jankowski, 1999a). This would suggest that a dysplastic mandible would be safe to biopsy.

The radiology of FD affecting the face and jaws gives an insight to its behaviour. Eversole's (1997) contention that the teeth in FD generally remain undisplaced without resorption, whereas COF may displace them or even resorb their roots is partly supported by a recent systematic review that found undisplaced over half of the teeth sited in dysplastic bone (MacDonald-Jankowski, 1999a). Akintoye and co-authors (2003) reported that FD did not distort the dental arch. Furthermore, Petrikowski and co-authors (1995) suggested that "alteration of the lamina dura to the abnormal bone pattern, and narrowing of the periodontal ligament space are primary distinguishing features" for FD. These phenomena in FD may reflect 'programmed field effect' of abnormal osseous development in congenitally predisposed bone matrix (Eisenburg and Eisenbud, 1997). This may account for the fusiform (spindle shaped) expansion of FD of the affected bone. In contrast, the

displacement of teeth or resorption of their roots in COF represents the almost spherical centrifugal expansion that is associated with a benign tumour growing out from the probable site of origin.

FD of the craniofacial complex may differ both radiologically and histologically from its counterparts in the axial skeleton. FD appears frequently in the latter as a circumscribed radiolucency with a thin sclerotic periphery, whereas cases of cranio-facial FD, certainly those affecting the jaws and adjacent bones, are poorer defined and more radiopaque. A reason for the difference in appearance between maxillofacial FD and FD of the long bones is that the former occurs in skeleton derived from membrane bone (Eversole, 1997). The woven bone, which is well mineralised, is arranged in a network of broad trabeculae. Furthermore, lamellar bone, generally absent in FD in the axial skeleton, occurs occasionally in FD of the face (Waldron, 1985; Slootweg, 1996), particularly in the monostotic form. FD commonly displays an abnormal opacification, which ranges from the very numerous, small and diffusely distributed opacities ['ground glass' and 'peau d'orange'] to sclerosis, classically described as 'cotton-wool'. Different patterns may not only be present in different parts of the same lesion, but may also depend on whether the film used is 'direct exposure' or 'fluorescent screen film' (Waldron, 1985).

The margins of extragnathic FD appear well-defined whereas they are poorly-defined in the jaws. An objective definition of marginal definition has been described by Slootweg and Müller (1990). A lesion with a zone of transition less than 1 mm

can be considered to be well-defined. This can be quickly and cheaply appreciated on plain film radiographs.

The expansion of FD of the mandible is classically spindle (or fusiform)-shaped when viewed on a true (axial) occlusal film or on a posterio-anterior projection of the mandible. Although the shape of the FD affected maxilla appears to be more complex, reflecting the maxilla's complex structure, the overall effect is similar to that seen on the mandible. The expansion of the external surface of the affected bone assumes a more grotesque but still recognisable shape, whereas the internal surfaces expand into orbital, nasal and sinus cavities, fissures, fossae and neural and vascular canals. The lesion, if large, often nearly completely obliterates the maxillary sinus. The above pattern is altered if the FD undergoes cystic degeneration with formation of a large aneurysmal bone cyst (ABC). Then the affected part of the lesion may lose its anatomical shape and becomes spherical (see Figures 2 to 4 of Ferretti and co-authors' report, 1999). At least some ABCs are neoplastic and since those affecting the maxillary are less likely to be reactive, then it can be appreciated that the multidirectional growth of the neoplasm will transform the typical FD presentation. Furthermore, the ABC may contain septae and fluid-fluid levels (Jundt, 2005b).

If FD affects the orbital cavity or more particularly the optic canal, then blindness can result. Although the onset of blindness is generally gradual and may be intermittent, urgent surgery is frequently required to recover sight (Ricalde and Horswell, 2001). If specialized surgeons are not available then corticosteroids may

help to alleviate optic nerve compression (Chapurlat and Meunier, 2000; Ricalde and Horswell, 2001).

Medical radiologists are familiar with an association between the ABC and FD. Although the ABC is a well-recognised accompaniment to FD of the skull base it is not of FD of the jaws. Examples of the radiology of ABC secondary to FD of the mandible and of the maxilla are illustrated by Dorfman and Czerniak (their Figure 8-24; Dorfman and Czerniak, 1998) and Lustig and co-authors (their Figure 2; 2001) respectively. Another concern particularly in long standing polyostotic FD is sarcomatous transformation, which can occur in absence of radiation therapy, 4% for patients with McCune-Albright, and 0.5% those with other FD forms (Cohen, 2000). Nevertheless, head and neck practitioners should be vigilant because the most frequent site for sarcomatous transformation is the craniofacial skeleton (Ruggieri et al., 1994). The features on conventional radiography, which suggest sarcoma may be differentiated from FD, are permeative ill-defined borders, destroyed cortical outline and/or spiculated periosteal new bone formation and widening of the entire periodontal ligament space (Petrikowski et al., 1995).

Prapayasatok and co-workers (2000) displayed in their Figure 3 a 'sunray' appearance in a case of FD, which disappeared on subsequent radiology 14 months later. This "sunray appearance could have been due to either an unusual pattern of calcification within the lesion or a periosteal reaction."

Jacobsson and co-authors' (1975) report is unique in that it relates inflammation to FD. Radiologically poorly-defined radiolucent areas within the FD appeared to be closely related to acute exacerbations and in many cases pain (on palpation) localized to these very areas. Although spontaneous remissions also occurred, most patients at some stage received antibiotics during these exacerbations, which in the majority appeared to relieve pain and prevent growth. The histology of biopsies presumably taken from these very sites only revealed woven bone typical of FOLs in 2 cases; only one case displayed inflammatory cells "making the diagnosis of chronic osteomyelitis questionable" presumably for this series. The accompanying commentary by Alling and Martinez (1975) considered these to represent reactive hyperplasia of bone.

Cemento-ossifying Fibroma

Ossifying fibroma (OF) and cementifying fibroma (CF) are now generally considered to be the two extremes of the same spectrum; because both frequently contain both bone and cementum-like tissue; these lesions are now called COF, the term adopted by the second edition of the WHO classification in 1992 (Kramer et al., 1992). The COF is a benign neoplasm, which is generally slow growing. Although it has principally been found in the jaws, it has also been reported in the frontal, ethmoid, sphenoid,' temporal' bones, the orbit, and the anterior cranial fossa.' (Som and Lidov, 1992)

The radiology of the COF in contrast to FD is well-defined and round or oval in shape. Ranging in presentation from radiolucent, central radiopacity/ies to completely opaque (MacDonald-Jankowski, 1998).

The COF exhibits a variable behaviour ranging from slow growth to occasionally aggressive local destruction; some cases recur after surgery (Wu et al., 1986a). Most COFs grow slowly and once completely excised do not recur, but a minority particularly in children (below 15 years of age; Waldron, 1995) exhibit rapid growth and a tendency to recur; the most frequent name applied to these lesions would appear to be 'juvenile ossifying fibroma' (JOF; Slootweg et al., 1994). Although this lesion is reasonably well-defined it may display erosion and invasion of adjacent bone (See Fig. 14-60; Waldron, 1995). The term JOF lesion may now represent two quite different lesions. Slootweg and co-authors (1994) first identified that the original WHO-defined JOF (JOF-WHO), those affecting the jaws of children and presenting without cemental or psammomatoid tissue, are true JOFs, whereas those occurring in adults, mainly in sinonasal (Slootweg et al., 1994; Eversole, 1997) and cranial bones (Eversole, 1997) and displaying cemental and /or psammomatoid tissue are actually COFs. Although Williams and co-authors (2000) have suggested that JOF-WHO bears some histological resemblance to osteofibrous dysplasia, an extragnathic fibro-osseous lesion, they could not identify the cytokeratin-positive cells of the latter in their JOF-WHO lesions. JOF occurs below 15 years of age, tends to recur and is reasonably well-defined. Regardless of the eventual taxonomy of this lesion, like the COF it requires surgical treatment. Furthermore, Brannon and Fowler (2001), not only report the presence of both types are varying sites and times

within the same lesion, but also in otherwise more conventionally behaving and appearing COFs. They add that, "because the initial treatment for ***all*** (their italics and bold text) OFs is assured complete surgical excision and because follow-up is recommended for all, the necessity of the diagnosis of "JAOF" (my comment: Juvenile Aggressive OF, a synonym for JOF) may be unwarranted." A need for long-term follow-up is evident in Meister and co-workers' (1973) report; all their 4 COFs followed-up for 18 years recurred.

Brannon and Fowler's (2001) use of the term OF instead of the hitherto COF reflects a growing movement that repudiates this lesion's previously purported periodontal ligament origin, instead, it arises from bone and that cementum-like structures are an expression of abnormal bone, having been found even in the extra-gnathic skeleton. Reichart and Philipsen also use OF in their 2004 textbook and Slootweg and El Mofty in the WHO's 2005 edition.

Canger and co-workers (2004) reported a familial case of COF affecting a father and daughter.

Another very rare but important manifestation of COF is the multiple form. Hwang and co-authors (2001) reported 5 rapidly growing separate COFs occurring in all four quadrants of the same patient over an 18-year period. Multiple COFs occurring in the jaws may mimic polyostotic FD (Khanna and Andrade, 1992).

Cemento-ossifying Dysplasias

Although there may be now little pathological (Eisenberg and Eisenbud, 1997) or radiological (Kawai et al., 1999; Ariji et al., 1994) rational for the once purported periodontal origin for most or perhaps even all of these lesions, there is little doubt that CODs are linked in some way to the presence of teeth (Melrose, 1997). They are almost exclusively confined to the alveolar process; in the mandible they are found superior to the inferior dental canal. This confinement to the alveolar process strongly suggests an odontogenic origin (Melrose, 1997). Kawai and co-authors (1999) observed 6 patterns of lesions. These lesions could broadly divided into two main types; those that were clearly in contact with the root or displayed hypercementosis, and those, which were separated from it by a radiolucent line that appeared to be continuous with the periodontal ligament space. They suggested the latter could have partly or wholly been derived from the medullary bone rather than from the pluripotential cells of the periodontal ligament. Their reason for this contention was that the mesial and distal aspects of the periodontal ligament space appeared normal on the radiographs. They did admit they were unable to determine the same for the buccal or lingual aspects, which cannot be displayed on conventional radiographs. Nevertheless, occlusal views display the COD located in the bucco-lingual centre of the mandible.

Follow-up of some of these cases suggest that very few individual lesions change from one pattern to another, although new lesions may arise in previously normal sites. Inspection of their Table 3 revealed that the latter occurred among the

youngest patients. This could suggest that in the majority of cases the condition developed on a lesion-by-lesion basis with increasing age until stability was achieved in old age. This would be consistent with the circumstantial evidence of such progression observed in another Oriental report (MacDonald-Jankowski, 1996a), solitary lesions were observed in the young adult age group, and multiple lesions unilaterally distributed in the middle age group, and the bilateral bimaxillary lesions in the oldest age group.

The second edition of WHO classification in 1992 recognises three separate COD entities, 'periapical cemental dysplasia' (PCD) (Waldron referred to this lesion as 'periapical cemento-osseous dysplasia' (PCOD; Waldron, 1993; Waldron, 1995), 'florid cemento-osseous dysplasia' (FCOD) and 'other cemento-ossifying dysplasia' (Kramer et al., 1992). The authors of the second edition recognised these categories "because it is useful to describe certain more or less well-defined clinicopathological presentations, without rejecting the possibility that they may be related to one another" (Kramer et al., 1992). According to Waldron (1993), "they appear to represent only variants of the same disease process". PCD and FCOD display multiple lesions. The 'other cemento-ossifying dysplasia' category includes all those CODs "which share some features of PCD or FCOD but do not have their characteristic clinicopathological patterns of presentation" (Kramer et al., 1992), such as the focal cemento-ossifying dysplasia (FocCOD), which is a solitary lesion (Summerlin and Tomich, 1994). Each separate or discrete lesion in all entities can display a similar range of presentations, ranging from largely radiolucent through increasingly opaque to complete opacification (Kawai et al., 1999).

When the lower incisors (which are classically vital) are only involved it is commonly called PCD whereas when two or more quadrants are affected then it is frequently diagnosed as FCOD. Classically the individual lesions of FCOD appears as lobular masses which may "attain a considerable size and cause expansion of the jaw", whereas those of PCD "rarely exceed 1 centimetre in diameter" (Kramer et al., 1992). Even before the WHO second edition blurred the distinction between PCD and FCOD, by claiming PCD can occur in posterior sites, PCD was shown in a very recent systematic review (SR) to have been used as a synonym for FCOD in a number of reports (MacDonald-Jankowski, 2003a).

Although the nomenclature for FCOD is extensive, the older and more general terms were more effective in recalling SR-included reports (MacDonald-Jankowski, 2003a). The term 'gigantiform cementoma' once a frequent synonym, still occasionally used, would appear to have been used in the literature first by Gorlin and co-authors (1961). Another old synonym, which still arises in connection with FCOD, is 'chronic sclerosing osteomyelitis'. Eisenberg and Eisenbud (1997) have suggested that this last term should no longer be applied to FCOD, because "no one has demonstrated that the osteomyelitic process is sclerosing". This of course does not exclude the possibility of chronic osteomyelitis occurring in a pre-existing FCOD.

The above SR (MacDonald-Jankowski, 2003a) reported that 59% of cases occurred in Blacks, 37% in Orientals and 2% in Caucasians (including Indians);

there was no difference in presentation between them. Cases in a report based more usually derived from histopathology files appear to be older than those in a report based on radiology-only files. Thus the generally reported older age of these lesions may reflect the fact that most remain symptom free and display no clinical signs which may indicate the surgery necessary to produce the pathological specimen (MacDonald-Jankowski, 2003a).

Both FCOD and PCD are most prevalent in women of middle to old age, 92% in the SR on FCODs (MacDonald-Jankowski, 2003a). This would suggest that, sex-linked factor/s are implicated in the aetiology. Furthermore, the mean age of the 5 male patients out of Kawai and co-authors' 54 CODs was 64.4 years compared to the females 49.4 (Kawai et al., 1999). This could suggest that female sex-linked factors do not only play a role in the high prevalence of this disorder among women but also in the development of these lesions at a younger age than in males. Although the mean age in women is broadly coincident with the onset of menopause, the absence of a gynaecological history in all reports means that this association should be considered to be circumstantial.

Although PCD disappears from the Reichart and Philipsen's (2004) textbook on odontogenic neoplasms, the PCD has now re-emerged as a subset of FocCODs within the WHO's 2005 edition (Slootweg, 2005). Although the exclusion of PCD as a specific entity is logical, because it is rare to find a case of PCD without also other COD lesions elsewhere in the jaws, Pippi and co-workers (1994) actually reported 7 cases of classical PCDs (affecting the lower incisors only) in White women of which

at least 5 were investigated additionally by panoramic radiographs, which would have displayed any other lesions in other sextants. They were followed up for 5 years and displayed no change either in appearance or a reduction of vitality of the pulp.

Once the diagnosis has been made, no treatment is indicated; surgery and tooth extraction are used only when the lesions became secondarily infected. This strategy minimises the frequency of post-operative complications and poor tolerance of mucosal-borne dentures.

The third type of COD, the single or solitary lesion of the focal cemento-ossifying dysplasia (FocCOD) is histologically indistinguishable from the individual lesions of FCOD and PCOD (Summerlin and Tomich, 1994). FocCOD like other CODs is more common in females. FocCODs have been reported in the Chinese (MacDonald-Jankowski, 1996). FocCOD can develop subsequently into PCOD and/or FCOD (Waldron, 1993; Summerlin and Tomich, 1994). Unlike PCOD and FCOD, radiological features of FocCOD are not sufficiently specific to differentiate them from small COFs (Waldron, 1995; Su et al., 1997a and b). Therefore, Melrose (1997) suggested a definitive diagnosis for CODs "is the gross appearance at surgery". When curetted, FocCOD produces, with difficulty, only a few scraps of tissue, whereas COFs are more readily shelled-out, because they "are sharply demarcated, encapsulated with an edge clearly separate from surrounding bone" (Melrose, 1997). Because of this difficulty in the pre-surgical diagnosis of FocCOD, particularly prior to its recognition as an entity entirely unrelated to COF may have resulted in surgery, which would now be considered to be unnecessary. As

a result FocCOD would appear to have become perhaps the most common FOL in pathology files (Waldron, 1995).

Although COD has a predilection for those of African or Oriental (East Asian) origin, a small number of Caucasian families display a clear autosomal dominant pattern (Young et al., 1989). Waldron (1995) called this form of COD 'familial gigantiform cementoma' (FGC). It affects both sexes equally and manifests at a younger age, as young as 4 years old (Young et al., 1989). FGC has been reported in a 16-year-old Japanese boy, his father and grandfather (Miyake and Nagahata, 1999). Unlike conventional COD FGC may undergo such extensive and even rapid expansion that surgery is required (Young et al., 1989). The Japanese boy experienced such florid growth of his lesions that over the 5 years after the initial diagnosis his lesions have advanced to severe deformity of both jaws (Miyake and Nagahata, 1999). The behaviour can vary from one individual to another in such a kindred, one displaying non-expansile lesions while others display substantial expansion (Waldron, 1995). The behaviour of the FGC can be so aggressive that it can on occasion be diagnosed as multiple COFs (Miyake and Nagahata, 1999). A family history may not always be available or ascertainable (Abdelsayed et al., 2001). A 20-year-old Chinese man presented with a 2-year history of progressive painless swelling of the mandible and pressure on the left eye. Radiographs showed that both jaws, including both antra were completely filled with COD lesions, only the symphysis menti and ascending rami were spared. No family history was given (Ong and Siar, 1997).

Although the vast majority of CODs requires no treatment, treatment is required when the COD lesion has become secondarily infected. Bencharit and co-workers (2003) report an edentulous case. The infection became so intractable that a hemi-mandibulectomy had to be performed followed by implants to achieve an adequate prosthodontic result.

An important association of the COD is the traumatic (simple) bone cyst (TBC; Horner and Forman, 1988). This appears as a moderately defined radiolucency, which in a dentate area displays 'scalloping', as its superior border (in mandibular TBCs) undulates around and between the roots. Classically the TBC displays little or no bucco-lingual expansion, but those associated with COD frequently exhibit bucco-lingual expansion and displace the inferior dental canal downwards (Matsumura et al., 1998). Furthermore, Melrose (1997) noted that that the classical TBC that affects teenage patients will generally heal completely after surgery, whereas those associated with CODs might not do so. Instead they are filled in by abnormal mineralised tissue similar to that of COD.

Millet (1990) reported one FCOD patient, a 48 year-old completely edentulous Black woman, presenting only with mild discomfort (but no ulceration) from one side due to denture-wearing displayed increased uptake of 99Tc-MDP and therefore activity in all COD lesions identified on a panoramic radiograph throughout the mandible and anterior maxilla. This "...increased osseous remodelling in absence of overt inflammation is suggestive of neoplastic or dysplastic behaviour."

A note on a potential development of COD's taxonomy; Slootweg and Mofty, (2005) recently used the term 'osseous dysplasia' in WHO's 2005 'classification of tumours'.

Chapter 2.

Introduction: THE HONG KONG CHINESE

Although the Hong Kong Chinese society appears modern and dynamic, creating the world's fifth busiest airport, ninth most active stock market and the longest rail and road bridge, it is still traditional with life centred on the patriarchal family.

Hong Kong is situated in the South China Sea on the South-eastern coast of China and has long been a gateway between China and the West. Its importance to the regional and world economy is disproportionate to its population (currently 6.725 million within an area of 1100 square miles (HK Government, 2002). Over the period covered by the studies in this thesis the Chinese proportion of the population has been in the order of 95-98% according to the censuses. (HK Government, 1981, 1991 and 2001)

Who are the Chinese?

Although the Chinese account for 22% of the global population, they are infrequently reported in the literature, particularly with regards to oral and maxillofacial disease. The Chinese constitute a distinct ethnic entity called 'Han'. This represents the cultural, linguistic, philosophical unity of those who consider themselves 'Chinese'. Not all Chinese according to political nationality are 'Han',

Tibetan, Mongolians and other minorities are not 'Han'. Furthermore, although there are differences in mitochondrial DNA between Han and Non-Han East Asians (such as Tibetans, Japanese and those of Indo-China; Qian et al., 2001), there is further a difference between Northern and Southern Han. (Chu et al., 1998). Almost all Hong Kong Chinese are Southern Han, the vast proportion originate from Guangdong (Canton), the adjacent mainland city and province.

Provision of dental services to the Hong Kong community

During the period of collection of the clinical data for this thesis the dental profession increased from 678 registered dentists in 1981 (when the Hong Kong's only dental school was opened) to 1358 in 1990, a 100.3% increase, in contrast to a 14.3% rise in population during a similar period. (HK Government, 1980, 1981, 1990, 1991) With the exceptions of a free provision for schoolchildren and a subsidised one for civil servants and their families (Mak et al., 1990), most of the population has to go to private general dental practitioners. This lack of a public dental service is compensated to some degree by a water fluoridation program that began in 1961 at 1.0 ppm and reduced to 0.7 ppm in 1978 when dental fluorosis became obvious (Evans et al., 1987). Currently, the overwhelming proportion of young residents in Hong Kong had been born there, and will have benefited from a reduction of caries, produced by water fluoridation (Wong et al., 2006).

This thesis is based on the assessment both of sequential cases from a Hong Kong community admitted to Prince Philip Dental Hospital (PPDH), and published

reports. The PPDH also houses Hong Kong's only dental school, the Faculty of Dentistry of the University of Hong Kong (UHK), since 1981. Surgery on the patients was performed within the above facility, or in the adjacent Tung Wah Hospital and from 1991 in the dedicated Oral and Maxillofacial Surgical facility, a then state-of-the-art in-patient unit, within the Queen Mary Hospital, the principal teaching hospital for the UHK Medical School. During this study there were 3 heads of Oral and Maxillofacial Surgery, the longest serving and thereby the most influential was Chair-Professor Henk Tideman, from 1989 to 2004. He established the firm routines under which the majority of patients reported in this thesis were managed. The histopathologist was Dr PC Wu, a medical trained pathologist who practiced as an oral pathologist on-site at the PPDH until 1996, when the Oral Pathology Unit, which she hitherto directed, was combined with the medical school's pathology unit.

The dental hospital and school registered 100,000 patients over the 10 years since opening in 1981. It provided a service to the community largely by way of treatment by students although an Oral Surgery service was available to referred patients for cysts and tumours. This was developed into a full oral and maxillofacial service after the arrival of Professor Tideman in 1989. The public health department was responsible for the first WHO standard dental survey in Hong Kong in 1984 under the leadership of Professor OP Lind (1987a & b) and repeated in 1991 under Professor E Schwarz (1994). Schwarz and co-authors reported an improvement in the short time since Lind and co-authors reported. Furthermore, a report by Ma, Mok, Islam, Li and MacDonald-Jankowski (2005) displayed a reduction of first molar loss

between 1983 and 1998, indicating reduced loss of teeth due to decay, but an increase in missing premolars and third molars reflecting an increase in both orthodontic and oral surgical treatments during the same period. These developments indicate the augmented and increasingly home-trained profession was having a positive effect of the dental health of the Hong Kong community. This increase in both generalists and specialists, particularly in Oral and Maxillofacial Surgery, practising in hospitals throughout Hong Kong, is likely to have resulted, in part, to the fall in the incidence of a range of lesions diagnosed at the PPDH in the preceding 10 years. (MacDonald-Jankowski, 2004 c and d)

Already known differences of radiologically apparent lesions affecting the jaws of the Hong Kong Chinese.

The formal oral pathological experience prior to the establishment of the HKU's dental hospital (PPDH) and school was expressed in print by a team headed by Wu (1985, 1986a and b). Many of the reports focusing on the radiology of many of these lesions were made by the present author.

Anatomical features that may reflect ethnic differences were taurodontism and calcification of the stylohyoid complex. Taurodontism was present in 46.4% of a young adult population and displayed a significant predilection for females (MacDonald-Jankowski and Li, 1993a). There are significant differences in the morphology patterns of calcification of the stylohyoid complex between Hong Kong and London; a calcified stylohyoid ligament is more prevalent in Londoners

(MacDonald-Jankowski, 2001a). The present author's 12 patterns of calcification of the stylohyoid complex are becoming the standard classification for this feature.

Lesions, frequently observed radiographically as incidental findings, such as the mucosal antral cyst (MAC), idiopathic osteosclerosis (IOS or dense bone islands), and the traumatic bone cyst (TBC, or simple bone cyst), were reported. The frequency of MACs in the Hong Kong Chinese was 5.2% (MacDonald-Jankowski, 1993a) comparing with 14.0% in a London inner-city population (MacDonald-Jankowski, 1994). The Chinese have a greater prevalence of IOS than British populations (MacDonald-Jankowski, 1999b). TBCs could be divided into a younger mixed gender group and an older exclusively female group; the latter displayed multiple TBCs (MacDonald-Jankowski, 1995)

Reports on benign odontogenic neoplasms affecting this community, which also systematically review the literature, include cementoblastomas, odontomas, odontogenic myxomas and ameloblastomas and. At least some cases for each of these lesions diagnosed in this community displayed differences in comparison to those reported in other communities. Of the 4 cases of cementoblastoma one uniquely arose from the furcation (MacDonald-Jankowski and Wu, 1992). The cases of complex odontomas appear to increase progressively in size in older age groups, suggesting continued growth (MacDonald-Jankowski, 1996b). The odontogenic myxoma in the Chinese displays more root resorption and tooth displacement than the rest of the SR (MacDonald-Jankowski et al., 2002); the frequency of root resorption is significantly less than that observed in ameloblastomas.

Ameloblastomas in the Chinese differed in a number of important respects to those of other communities. It has a younger age of first presentation, a shorter period between first becoming aware of the lesion and seeking treatment and is more associated with pain and has a higher proportion of unicystic forms (MacDonald-Jankowski et al., 2004c and d)

In conclusion, the Hong Kong Chinese display features in a broad range of lesions and anatomical entities differing from those observed in other communities.

Traditional Chinese Medicine

Much 'traditional Chinese medicine' (TCM) has clear pharmacological effects, which are used efficaciously to treat certain diseases (Linde et al., 2001), but also can complicate delivery of Western dentistry (Little, 2004) and medicine (Lee et al., 2006; Little, 2004). "Patients taking aspirin, warfarin, ticlopidine, clopidogrel, or dipyridamole should not take ginkgo biloba, because bleeding may occur (Little, 2004)." Lee and co-authors (2006) reported an increased partial prothombopastic time and hypokalaemia perioperatively with TCM.

Many if not most of the patients, the subjects of this thesis, were diagnosed at a time when the attitude to TCM was still strong. Although today, its use is greatest among the poorer, older cohort, particularly females (Chan et al., 2003), its use is still common among Hong Kong medical students (Hon et al., 2005). Tang and

Wong (1998) observed that TCM is more popular among the Hong Kong Chinese than it is among the Taiwanese or the mainland Chinese.

The Hong Kong Chinese generally view their health in a macrocosmic way (they are aware of the potential of multifactorial elements, including environmental factors, to affect the disease process) in contrast to Western medicine's traditional reductionist approach to a disease. (Koo, 1987) Treatment in TCM is based on maintaining Qi (pronounced and also written as Chi), the equilibrium for health or life, which balances the two universal cosmic forces Yang (male, strong or hot) and Yin (female, weak or cold). The interaction of these two cosmic forces produces the five elements from which all things are created. Disease is believed to occur when Yang and Ying are no longer in balance. This can be actively restored by ingesting the deficient, and/or eliminating the excess Yang or Yin or simulating the malfunctioning organ is some way (acupuncture, moxibustion or massage). But this is not all; an important element of the treatment is the practitioner. It is important that the practitioner is 'predestined' for that patient with his or her particular complaint. Therefore, if the treatment does not appear be working after a few doses the patient will seek another practitioner, even if the existing one enjoys an excellent reputation. Today in Hong Kong this shopping-around in not merely confined to traditional Chinese medical practitioners, but also to doctors and dentists. (Lee et al., 1993) This can make it potentially difficult to observe and follow-up slower growing lesions, particularly those that do not cause pain.

The Hong Kong Chinese attitude to disease is flexible, when the lesion is painful and acute, Western medicine is preferred; nearly 99% of hip-fractures are hospital treated (Schwartz et al., 1999). If the lesion is not painful, then the patient may first resort to TCM.

An unknown element of TCM is the long-term effects of its prescription on biological systems. The differences observed in this southern Chinese population may be caused in part by TCM. Any contribution to the presentation or conduct of FOLs of the jaws remains unclear.

Chapter 3.

Introduction: SYSTEMATIC REVIEW

Preamble and introduction.

Central to a systematic review (SR) is the establishment of a research question, selection criteria, a search plan, a literature search, an appraisal of the identified literature by the selection criteria; an analysis and a formulation of recommendations. SR is now considered a form of research, requiring the same scientific method well-established in medicine, with information on reviews available in several databases, including the 'Cochrane Database of Systematic Reviews'. Although generally applied to clinical trials, in particular randomized controlled trials (RCTs), SR can be employed in studies in oral and maxillofacial radiology, where observational studies are generally only possible. Radiologists (Rohlin and Mileman, 2000) have already begun to make an impact in dentistry by using SR as a decision-making tool. The present author has already published a 2-part series with a medical informationist at the University of Edinburgh at the invitation of the *Asian Journal or Oral and Maxillofacial Surgery* (MacDonald-Jankowski and Dozier, 2003 b and c)

A SR of a radiological topic provoked much comment in the international medical community in 2001 when Gotzsche and Olsen (2000) questioned whether screening for breast cancer by mammography was entirely justifiable. SR has been

defined as a summary of the medical literature that uses explicit methods to search systematically, appraise critically and synthesize the world literature on a specific issue. Its goal is to minimise both bias and error. SRs may, but need not, include some statistical methods for combining the results of individual studies and we will call this subset 'meta-analysis' (Sackett et al., 2000). SR aids rather than replaces clinical reasoning. It guides health policy by influencing good practice and directing research since existing data is summarized, hypotheses refined and sample sizes estimated (Cook et al., 1998).

SR is increasingly preferred to the traditional narrative review because it is more objective and renders the review process transparent (Egger and Smith, 1997; Greenhalgh, 1997a). It tries only to include studies, which have a low susceptibility to bias. It must include a 'Materials and Methods' section, which defines strategies used to avoid bias. The usual SR sequence has 7 steps (see Stroup and co-authors (2000) for a more detailed checklist). The reviewer should document each of these steps in the published review, providing all the details required to reproduce the review.

Step 1: Form the research question

The research question, or questions, on which the search strategy is then based, should have four components. They are frequently not fully expressed but readily implied from the text. This is particularly so in radiology which is central to almost every aspect of dentistry' (Hirschmann, 1993) where the principles of its use

are generally well understood. These questions are now frequently called PICO questions. These state the 'primary problem' (P), 'intervention' (I), 'comparison' (C), 'outcome' (O).

Problems arise when the general readership is unfamiliar with the principles of radiology, particularly mammography in the case of the paper by Gotzsche & Olsen (2000). Furthermore, Gotzsche & Olsen (2000), non-radiologists, were unable to appreciate that the system of SR applied to it was entirely inappropriate. This will be discussed further later.

Step 2: Appoint selection or eligibility criteria

Once the research questions have been defined, it is easier to determine the selection, or eligibility, criteria by which the body of relevant literature will be sifted (Counsell, 1998). These criteria could be 'inclusion' or 'exclusion' (see Arrive and co-authors' (2000) more extensive subclassification of selection criteria). It is important to define the width of these criteria; narrow criteria could exclude relevant studies and wide criteria could include studies using quite different methods, increasing the risk of heterogeneity. The characteristics of a database search are 'recall' (or comprehensiveness) and 'precision'. Therefore, a search with a high recall and low precision may produce an unmanageable number of studies, many of them irrelevant to the subject of the SR (Decks et al., 1996). Nevertheless, it is generally preferable to move more towards recall because irrelevant reports can be

discarded, (Goodman, 1993) whereas overemphasis on precision may exclude relevant material.

Bias

Although a major aim of SR is to minimize bias, it is, like any other area of research, subject to it. There are many sources of bias in SR. The reviewer has little control over some of these, such as publication or database bias. Other means must be used in order to overcome these. Those over which he/she does have control include 'language bias', 'inclusion bias' and 'reviewer bias'. 'Publication bias' reflects the bias of journals towards certain reports; those producing positive results are more likely to be published. 'Database bias' reflects the bias of the index compilers to English language journals but against journals originating from the developing world; only 2% of the latter are indexed. Although almost all of the 1861 Indian journals are published in English, only 30 are indexed (Egger and Smith, 1998).

'Reviewer bias' is important, because the inclusion criteria selected depend upon the knowledge of the reviewer. De Konig's commentary (2000) implied that as Gotzsche and Olsen (2000) had not specialized in radiology, particularly in mammography, this affected their choice of selection criteria and therefore their results. But ignorance of the literature to be reviewed could be an advantage because of 'inclusion bias', where a reviewer uses his/her knowledge of the literature to manipulate the criteria so as to exclude reports reaching conclusions with which

he/she does not agree. This affects the validity of the SR (Goodman, 1993) and is a major reason why the selection criteria should be determined before the literature search begins. However the width of the selection criteria may need adjustment after the data has been identified, because it is dependent on the quantity of relevant papers identified: criteria may be found in retrospect to be too narrow or too wide (Counsell, 1998). Any such adjustment must be fully explained in the text. Another important source of 'inclusion bias' is 'competing interests', which if not expressly declared, may on occasion be inferred by the author's affiliation and funding.

Step 3: Formulate a search plan

A literature search must be based on a written 'search plan': what key words will be used; which databases should be searched; whether electronic or printed or both; whether 'English language only' is to be reviewed (as used recently by Bryant and co-authors, 2007 on osseointegrated implant outcomes); the category and subject areas of journals to be hand-searched; what areas of the 'grey literature' are to be considered. An important aspect of the planning will take account of the reviewers' resources, because hand-searching in particular is labour-intensive and time-consuming and therefore expensive. This 'search plan' is set out in the 'Materials and Methods' section. The reader can determine whether the plan was appropriate and whether it is reproducible.

Step 4: The literature search

The primary search will be based on medical databases.

(a) Databases

(i) Electronic Databases:

Biomedical journals are indexed in many electronic databases, of which the most frequently used are Medline, Embase and Web of Science. Medline (Index Medicus on-line; National Library of Medicine) is the best-established database, with about 9 million records from 3900 journals published since 1960; 80% of the indexed articles are in English (Allison et al., 1999). Embase (Excerpta Medica on-line: Elsevier Science) has over 5 million records from more than 4000 journals since 1974. About 1000 Embase journals are not included in Medline (Counsell, 1998). Although Embase has a shorter indexing delay (4-8 weeks) than Medline (3-6 months), this has now been partly addressed by 'PreMedline', which includes simple records for articles, even before publication, based on information sent by publishers (Greenhalgh, 1997). Embase is notable for its coverage of pharmacology with very good indexing of European language journals (Greenhalgh, 1997a) but has fewer dental journals. Almost all dental and maxillofacial journals it indexes are already in Medline.

The potential reviewer should appreciate that the printed versions Index Medicus and Excerpta Medica go back to 1879 and 1945 respectively. The National

Library of Medicine has already begun to address the incompleteness of Medline in relation to Index Medicus by producing 'OldMedline'.

Although the 'Science Citation Index (ISI: Institute for Scientific Information) Expanded' has records from over 5700 journals, only a fraction are bio-medical. The version available to the higher education community and hospitals is the 'Web of Science', which goes back to 1945. Science Citation Index is notable for its 'cited reference search'. This function allows the researcher to find articles, which cite a known article.

A useful database for those literate in Romance languages is 'LILACS', the literature index for Latin-America and the Caribbean created by the Biblioteca Regional de Medicina (BIREME); it covers 700 biomedical journals of which only 41 overlap with Medline or Embase. LILACS can be searched in English.

Two major problems face the reviewer in searching these databases. The first, already mentioned, is the problem of language. To adhere to the central aim, to "systematically search, critically appraise and synthesize the world literature on a specific issue" (Sackett et al., 2000) for a thorough systematic review, the ability to translate is essential. The second problem is that of funding for access to commercially produced databases. Thanks to the US government Medline is free to the world as PubMed. Embase and Science Citation Index, and almost all other databases, are only available at a charge.

(ii) Elements of electronic search

The literature search is broadly similar to a routine literature search for clinical information (see Greenhalgh, 1997), except that it is systematic and rigorous. It can use controlled subject headings or index terms (such as MeSH or Emtree of Medline and Embase respectively), and free-text terms.

Controlled subject headings

Subject headings are listed in a 'thesaurus' or 'controlled vocabulary' and are used by indexers to describe the content of articles. The indexers only use the listed terms - they do not make up new ones - which is why they are called 'controlled'. MeSH (Medical Subject Heading) terms are 14000 specific terms and 180000 synonyms. A MeSH term is assigned to each identified topic (Mulrow and Cook (1998). It should be noted that the main purpose of MeSH for the print version of 'Index Medicus' is to assist indexing and cataloguing, but a separate list has been formulated especially for searching Medline.

MeSH is organized in a browseable hierarchy, from broader to narrower. It is possible to navigate the index hierarchy to see where a given subject heading is placed, to see what broader subjects are above it and what narrower subjects below. The indexers use the most appropriate subject headings, but these are not always the most relevant, appropriate, or precise for dentistry. In dentistry it is therefore necessary to use broader subject headings than would at first seem appropriate.

'Exploding' and 'free-text searching'

When a subject heading and all narrower headings below it are relevant, it is easiest to 'explode' that broader heading. Rosenfeld (1996) advises that MeSH searches should be supplemented by a 'text-word' (a word that appears in titles and abstracts) search. This free-text search (a search using a 'text-word') does not consider the context in which the term appears, so may result in irrelevant hits. In addition to performing a 'free-text' search for each subject heading, all variants, alternative spellings or synonyms should be included. The subject heading indices are revised regularly to reflect developments, but nonetheless, sometimes there is no appropriate heading for new or unusual terms, in particular in the smaller research fields such as dentistry and radiology. In these cases 'free-text search' is the only option. Ironically, this also applies to the term 'systematic review', a 'text-word' whereas its subset 'meta-analysis' has been a MeSH term since 1989.

(b) Hand-searching and reference or citation lists

Although correct cataloguing is absolutely central to indexing of the databases, it is claimed that up to 50% of all Medline records are miscataloged (Greenhalgh, 1997b). A way to counter this error is to hand-search all the journals relevant to the search and review carefully the references of all papers identified in the databases (Counsell, 1998; Dickersin et al., 1994). The list of journals hand-searched for all four lesions in this thesis is set out in Table 3.1.

Table 3.1. Medline-indexed journals: Hand-searched

e, e-journal: These journals are subscribed to only in the e-journal format by the UBC libraries. The 'years hand-searched' reflects the years during which the UBC libraries subscribed

Subject area	Journals hand-searched	Years hand-searched
Medical & Oral and Maxillofacial Radiology	Radiology	1971-2007
	Dentomaxillofacial Radiology	1989-2007
	Clinical Radiology	1971-2007
Oral & Maxillofacial Surgery (OMFS)	Journal of Oral & Maxillofacial Surgery	1971-2007
	International Journal of Oral & Maxillofacial Surgery	1972-2007
	British Journal of Oral & Maxillofacial Surgery, e	1980-2004
	Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics	1971-2007
	Mund-, Kiefer- und Gesichtschirurgie, e	1997-2007
	Revue de stomatologie et de chirurgie maxillo-faciale, e	1999-2007
Otolaryngology	Asian Journal of Oral & Maxillofacial Surgery	2003-2007
	Journal of Otolaryngology	1972-2007
	Journal français d'oto-rhino-laryngologie; audiophonologie et chirurgie maxillo-faciale	1971-1986
	Annales d'oto-laryngologie et de chirurgie cervico faciale: bulletin de la Societe d'oto-laryngologie des hopitaux de Paris, e	1997-2007
Oral Pathology	Journal of Oral Pathology & Medicine	1972-2007
	Oral Diseases, e	2001-2007
Other	Journal of Dental Research	1971-2007
	Oral Oncology, e	1998-2007

(c) Grey literature

The 'grey literature' refers to literature not published in journals or commercially published books. A problem with the gray literature is the increased risk of duplicating the same reports as those identified by the database search, as half proceed to full publication (Counsell, 1998).

Step 5: Appraise the identified literature by selection criteria

Once the relevant literature has been identified, the next step is to apply the predetermined selection criteria in order to include or exclude papers from the systematic review. Blind and independent assessment of the data has been advocated to avoid 'reviewer bias' which influences the acceptance or rejection of borderline reports. Such decisions, whether to include or exclude contentious reports, (as illustrated by Bryant and co-authors' (2007) SR, commissioned the Academy of Osseointegration), were by consensus. This SR was then reviewed, by an expert panel, for its accuracy and completeness.

Step 6: The analysis

The appropriate statistical techniques are applied to combine the reports included in the review. There is an extensive literature in radiology on such tests (Greenhalgh, 1997c; Greenhalgh and Donald, 2000) Nevertheless, there are many biases intrinsic to radiology, in particular 'verification bias', which is very frequent

in studies of diagnostic performance. It significantly affects sensitivity and specificity (Kelly et al., 1997).

Step 7: The formulation of recommendations

"SR . . . could help decision makers cope with information overload" (Jadad et al., 2000). The recent application of SR has allowed two radiologists, Rohlin and Mileman (2000), to comment on a diverse range of dental studies.

Conclusion

As all systematic reviews are retrospective, they are subject to systemic and random errors. Therefore, their quality depends on the extent to which the methods of scientific review described above have been used to minimize error, in particular bias. SR is increasingly important in our current evidence-based culture. The Cochrane Collaboration has already moved beyond RCT to index observational SR, although not as yet diagnosis and therefore not radiology, nevertheless because of their position at the heart of dentistry, radiologists have already begun to make an impact by using SR as a decision-making tool.

Chapter 4.

FLORID CEMENTO-OSSEOUS DYSPLASIA

INTRODUCTION

Florid cemento-osseous dysplasia is a well-recognized lesion predominantly affecting middle-to-old aged Black women. Once diagnosed, treatment is not generally necessary. The term 'florid cemento-osseous dysplasia' (FCOD) has been proposed in the second edition of the WHO's 'International histological classification of odontogenic tumours' (Kramer et al., 1992) to replace the first edition's 'gigantiform cementoma' (Pindborg et al., 1971). FCOD is defined as "Lobulated masses of dense, highly mineralised, almost acellular cemento-osseous tissue typically occurring in several parts of the jaws..."(Kramer et al., 1992). Although the second edition essentially upheld the first edition's definition of FCOD, it modified the first edition's definition of periapical cemental dysplasia (PCD; Pindborg et al., 1971), another 'cemento-osseous dysplasia' (COD), which "mostly [affected] mandibular incisors" to "which may be adjacent to one another or in different parts of the jaws" (Kramer et al., 1992). The problem with this is that it confuses the boundary between FCOD and PCD, if they are indeed two distinct lesions. The WHO definition only refers to the end-stage for FCOD, but considers the natural history of PCD including initial radiolucent and final "dense mineralized mass" stages. Furthermore, PCD need not be multiple, as the definition clearly recognises that PCD can affect single teeth. The sole point that appears to separate

FCOD and PCD is that for PCD "Each periapical lesion is self-limiting, rarely exceeds 1 cm in diameter..." (Kramer et al., 1992). By creating a separate category of "other cemento-osseous dysplasias" for those "lesions, which share some of the features of periapical and/or florid cemento-osseous dysplasia, but do not have their characteristic clinicopathological patterns of presentation", the authors of the second edition (Kramer et al., 1992) accepted that further development in this area is required. Since the publication of the second edition, two other types, which did exist prior to its publication, have become largely accepted. They are Waldron's 'familial gigantiform cementoma' (FGC; Waldron, 1995) and his 'localized fibro-osseous-cemental lesions' (Waldron, 1985), renamed 'focal COD' (Summerlin and Tomich, 1994; Su et al., 1997b). The former predominantly affects more than any one individual of either gender and of any age of the proband's siblings or parents.

The second edition's qualification that "Black persons are affected more commonly than Caucasians, and sometimes there is a familiar distribution" (Kramer et al., 1992) cannot be considered immutable, as the occurrence of this lesion in Orientals was relatively unreported at the time of the second edition. Indeed, their words "more commonly" and "sometimes" make it clear that this sentence is advisory rather than forming part of the definition.

CODs will be reported in two chapters; the first chapter (Chapter 4) will address FCODs and the second (Chapter 5) will the Focal CODs (FocCODs). Chapter 4 will be further divided into two parts; the first will address the clinical and radiological presentations of FCOD in that Hong Kong Chinese community

attending PPDH. The second part will address the search terms and electronic databases chosen for the SR. it will consider a SR of all FCODs.

AIMS AND RESEARCH QUESTIONS

The primary research question for this SR, or PICO question, is "Do other clinical and radiological features improve diagnosis of FCOD compared with multiple FOLs affecting more than 1 sextant?"

In order to answer this question only those reports, which consider multiple lesions affecting more than one sextant as a FCOD, can be admitted to this SR. Such lesions need not be histopathologically confirmed as FOLs; series of cases based solely on radiology will be considered for inclusion. In addition to this question there are other supplemental questions, which help to frame the selection criteria for the above PICO question; these are: -

Question 1: What are the clinical and radiological characteristics observed in a largely Southern Chinese Hong Kong community?

This requires a detailed analysis of the clinical and radiological features observed in a continuous series of cases of FCODs in a Hong Kong Chinese community admitted to PPDH.

Question 2: Do Hong Kong Chinese/Oriental communities have a different presentation of FCOD compared with non-Chinese/Oriental communities?

Comparison of the Hong Kong Chinese with the rest of the SR will be addressed in this chapter. Comparison of the Oriental communities with regards to other global communities will be addressed in Chapter 8. To assist the formulation of an answer the SR-included reports will be divided into four global groups, Western, African, Oriental and Latin-American, broadly reflecting ethnic origin.

Question 3. "Do reports based on histopathology files have a different presentation of FCOD compared with those based on non-pathology sources, such as radiology-only files?"

Included in this SR are the findings of two reports on FCOD on the Hong Kong Chinese; the first derived from a radiology-only file (MacDonald-Jankowski; 1992a) and the second from a histopathology file (MacDonald-Jankowski; 1995)

Question 4. Which search terms are most effective for searching for reports on FCODs?

MATERIALS AND METHODS

A: Radiology-only and Histopathological-file-based cases of FCODs affecting the Hong Kong Chinese.

The radiology-only file-based report was based on the 'interesting cases' book, which was kept in the reporting room of the Oral Radiology Unit, whereas the cases derived from the histopathology files were indexed in the Oral Pathology Unit.

Cases in both groups were searched for under the following terms; PCD, GC, FOD, and FCOD. 'Sclerosing osteomyelitis' an additional search term, was confined to the histopathology-file-based report. Panoramic radiographs were available in all cases, and in some cases, periapical and occlusal radiographs were also available. The radiographs were reviewed on standard viewing boxes sited in reduced ambient lighting. All lesions were situated within the alveolar process; the inferior dental canal arbitrarily set the lower border of the posterior aspect of the alveolar process.

To answer 'Question 2,' the 23 search terms were derived from textbooks, periodical articles and both editions of the WHO's classification of odontogenic tumours. The search terms used (Table 4.1) were synonyms for FCOD, PCD and COD in general; 'Diffuse Sclerosing Osteomyelitis' is not a synonym *per se* for FCOD, but has been included because it contributes to the discussion. The only MeSH term relevant to the SR was 'Cementoma'. [Search terms in this report will be quoted in full, in parenthesis and with upper case initial letters, e.g. 'Florid Cemento-Osseous Dysplasia'.]

B: Systematic review

A SR is required to answer the PICO question. A SR requires not only a literature to search, but also selection criteria to sift this literature. As the primary aim is to include as many reports as possible a wide search of the literature will be made, including non-English reports.

Selection criteria.

There were 3 inclusion (Criteria 1 to 3) and 1 exclusion (Criterion A) criteria for the SR. Each report will pass through these criteria in strict sequence. Although a report may be excluded by more than one criterion, only the first criterion to exclude a particular report will appear in Table 4.5. [For the sake of brevity only those reports that cannot be readily identified from their title or abstract will be discussed and cited.]

'Exclusion' refers to the 'non-inclusion' of a report within the SR and will be used regardless of whether it is in relation to either 'inclusion' or 'exclusion' selection criteria.

Criterion 1. The study should be consistent with the WHO definition of FCOD.

The study had to be consistent with at least the first edition of the WHO'S histological classification of odontogenic tumours (Pindborg et al., 1971). This edition described 'Gigantiform Cementoma' as multiple, often-symmetrical masses of cementum typically occurring in several parts of the jaws (derived from text and table). The word "often" was interpreted as advisory, but the words "multiple" and "typically" were essential to the definition. The second edition's (Kramer et al., 1992) use of "sometimes" with reference to "familial" was only advisory and appeared to apply subsequently to FGC, a separate lesion with entirely different clinical manifestations and behaviour and was not subject of this study. Reports

composed wholly of FGC or likely to include in excess of 10% of FGC in their reports were excluded. Furthermore, hypercementosis was expressly excluded from the definition.

Criterion 2. Clear evidence that multiple sextants had been reviewed for CODs to make the diagnosis of FCOD.

FCOD has been widely defined for the purpose of this study as multiple lesions occurring in more than one sextant. As the pattern of these multiple lesions should be observable on radiographs that are generally considered adequate for diagnosis, radiology-only studies without histopathological confirmation were admitted in order to determine whether there were any differences in presentation between histopathology-file-based and radiology-only reports. An absence of the likelihood of that the whole of the jaws had not been conventionally radiographed would exclude those reports. This criterion is necessary to determine between FCODs, and FocCODs.

To achieve the maximum inclusion of reports, those reports considered for exclusion under Criteria 2 were researched for earlier and perhaps fuller reports in theses or local journals that may provide more essential details that could salvage them. Because the diagnosis of FCOD is dependent on radiography of the whole jaws, reports that cannot provide radiographic details for *all* their cases can nevertheless be partially salvaged and included in the SR if the cases that have radiographs displaying the complete jaws can be readily identified.

Criterion 3. The study should represent a complete collection of cases of FCOD occurring in the reporters' caseload.

The study should represent a complete collection of cases of COF, arising within a particular community, occurring in the reporters' caseload. Reports that were merely a selection of cases such as case reports and those studies, which were primarily concerned with specific investigations or a discrete age group, such as children or a particular jaw, were excluded.

Generally, reports with less than 3 cases were considered to be cases reports and thus excluded unless it was clear that they represented a complete consecutive series; this could be implied from the FCODs appearing in a report on consecutive FOLs.

Criterion A. Exclude reports whose data have already been reported and included in the SR.

Generally the largest and most detailed reports will be chosen over the lesser.

Database interrogation, hand-searching and reference-list harvesting

To determine the relative inclusiveness (or 'Recall') of 2 major databases in 2003, (MacDonald-Jankowski, 2003) the search terms derived from alternative

nomenclature for FCOD were used to interrogate Medline and ISI Web of Science. Medline contains medical articles from 1960 and is available free using the PubMed interface. The version of Web of Science used in this study goes back to 1945 and reviews a different selection of journals.

Medline and Web of Science were interrogated by the search terms (see Table 4.1.). This was supplemented by a hand-search of those journals listed in Table 3.1. This strategy was further augmented by 'reference-list harvesting' of the bibliographies (or citation lists) of all reports identified by the databases or hand-searching. The bibliography of the SR-included reports is set out in Table 4.2.

"Recall" and "precision" for each search term and database were defined and displayed in Table 4.1 as percentages. Recall was expressed in SR-included reports for that search term for that database as a percentage of the total number of SR-included reports. Precision was expressed in SR-included reports as a percentage of the total number of reports for that search term for that database.

A search was performed on LILACS using the same search terms.

Definition of parameters.

The number of years is calculated on the assumption the study begins on the January of the beginning year and ends on the December of the closing year unless stated otherwise in the text.

The 'number of FCODs per hospital per year' reflected the number of hospitals contributing to the report and the number of years from which the reported series was derived (MacDonald-Jankowski, 2003a).

The jaws were further divided into posterior (molar and premolar) and anterior (incisors and canines) sextants. Although the demarcation point between these areas was infrequently expressed, it was taken to occur at a vertical line just distal to the distal surface of the canine.

The lower border of the mandibular alveolus is set by the inferior dental (mandibular) canal and the upper border of the maxillary alveolus on panoramic radiographs is set by the image of the hard palate on panoramic radiographs or lateral cephalographs (MacDonald-Jankowski, 2004a).

Significant differences in frequencies were tested by the X^2 test with $P < 0.05$. Significant differences in age were tested by a Student' t-test with $P < 0.05$.

Table 4.1. Florid Cemento-Osseous Dysplasia: Search terms; Medline and Web of Science

Search Terms	Total Number of Reports		Number of reports Included in the SR		Recall (%)[a]		Precision (%)[b]	
	Medline	Web of Sci.	Medline	Web of Sci.	Medline	Web of Sci.	Medline	Web of Sci.
(a) Florid Osseous Dysplasia	42	21	5	5	31.2	31.2	11.9	23.8
(b) Florid Ossifying Dysplasia	8	0	0	0	0	0	0	0
(c) Florid Cemento-Osseous Dysplasia	19	11	2	0	12.5	0	10.5	0
(d) Florid Cemento-Osseous Dysplasia	2	0	0	0	0	0	0	0
(e) Gigantiform Cementoma	25	25	6	5	37.5	31.2	24.0	20.0
(f) Familial Multiple Cementomas	2	0	0	0	0	0	0	0
(g) Periapical Cemental Dysplasia	40	13	5	1	31.2	6.2	12.5	7.7
(h) Periapical Cemento-Osseous Dysplasia	14	2	1	0	6.2	0	7.1	0
(i) Periapical Osseous Dysplasia	25	0	4	0	25.0	0	16.0	0
(j) Periapical Fibrous Dysplasia	26	1	3	0	18.8	0	11.5	0
(k) Benign Periapical Fibroma	10	0	2	0	12.5	0	20.0	0
(l) Cemento-Osseous Dysplasia	30	23	2	0	12.5	0	6.7	0
(m) Cemento-Ossifying Dysplasia	11	0	1	0	6.2	0	6.2	0
(n) Multiple Enostosis	8	2	1	1	6.2	6.2	12.5	50.0
(o) Multiple Endostosis	0	0	0	0	0	0	0	0
(p) Sclerosing Osteitis	12	5	2	1	12.5	6.2	16.7	20.0
(q) Sclerosing Osteomyeliis	162	124	4	1	25.0	6.2	2.5	0.8
(r) Chronic Sclerosing Osteomyelitis	108	38	2	1	12.5	6.2	1.8	2.8
(s) Diffuse Sclerosing Osteomyelitis	54	56	2	0	12.5	0	3.7	0
(t) Periapical Osteopetrosis	4	1	0	0	0	0	0	0
(u) Benign Fibro-Osseous Lesions of Periodontal Ligament Origin	5	1	2	0	12.5	0	40.0	0
(v) Cementoma	243	48	7	6	43.8	37.5	2.9	12.5

Search Terms	Total Number of Reports		Number of reports Included in the SR		Recall (%)[a]		Precision (%)[b]	
	Medline	Web of Sci.	Medline	Web of Sci.	Medline	Web of Sci.	Medline	Web of Sci.
(w) Osseous Dysplasia	418	118	9	4	56.2	25.0	2.2	3.4

Abbreviations and Notes: [a] , Recall was expressed as SR-identified reports for that search term for that database as a percentage of the total number of SR-identified reports, which is 16; [b] , Precision was expressed as SR-identified reports as a percentage of the total number of reports for that search term for that database. The databases were also interrogated by all search terms on 31st January 2003. and presented as published in Dentomaxillofacial Radiology 2003 (MacDonald-Jankowski, 2003)

Table 4.2. Florid cemento-Osseous Dysplasia; Systematic review; Bibliography of included reports.

Search Terms	Medline	Web of Science
(a) Florid Osseous Dysplasia	MacDonald-Jankowski, 1996 Melrose et al., 1976 Groot et al., 1996 Miyamoto, 1996 Lahbabi et al., 1998	MacDonald-Jankowski, 1992 MacDonald-Jankowski, 1996 Melrose et al., 1976 Loh and Yeo, 1989 Groot et al., 1996
(b) Florid Ossifying Dysplasia	None	None
(c) Florid Cemento-Osseous Dysplasia	Miyamoto, 1996 Lahbabi et al., 1998	None
(d) Florid Cemento-Osseous Dysplasia	None	None
(e) Gigantiform Cementoma	MacDonald-Jankowski, 1992 Melrose et al., 1976 Loh and Yeo, 1989 Thompson and Altini, 1989 Ogunsalu et al., 2001 Matzuzaka et al., 2002	MacDonald-Jankowski, 1992 MacDonald-Jankowski, 1996 Waldron et al., 1975 Thompson and Altini, 1989 Groot et al., 1996
(f) Familial Multiple Cementomas	None	None
(g) Periapical Cemental Dysplasia	Neville and Albenesius, 1986 Tanaka et al., 1987 Miyamoto, 1996 Ogunsalu et al., 2001 Matzuzaka et al., 2002	Ogunsalu et al., 2001
(h) Periapical Cemento-Osseous Dysplasia	Miyamoto, 1996	None

Search Terms	Medline	Web of Science
(i) Periapical Osseous Dysplasia	Neville and Albenesius, 1986 Saini, 1991 Miyamoto, 1996 Matzuzaka et al., 2002	None
(j) Periapical Fibrous Dysplasia	Groot et al., 1996 Ogunsalu et al., 2001 Matzuzaka et al., 2002	None
(k) Benign Periapical Fibroma	Neville and Albenesius, 1986 Ogunsalu et al., 2001	None
(l) Cemento-Osseous Dysplasia	Miyamoto, 1996 Lahbabi et al., 1998	None
(m) Cemento-Ossifying Dysplasia	Matzuzaka et al., 2002	None
(n) Multiple Enostosis	Waldron et al., 1975	Waldron et al., 1975
(o) Multiple Endostosis	None	None
(p) Sclerosing Osteitis	Waldron et al., 1975 Loh and Yeo, 1989	Waldron et al., 1975
(q) Sclerosing Osteomyeliis	Waldron et al., 1975 Loh and Yeo, 1989 Saini, 1991 Lahbabi et al., 1998	Waldron et al., 1975
(r) Chronic Sclerosing Osteomyelitis	Waldron et al., 1975 Lahbabi et al., 1998	Waldron et al., 1975
(s) Diffuse Sclerosing Osteomyelitis	Saini, 1991 Lahbabi et al., 1998	None
(t) Periapical Osteopetrosis	None	None

Search Terms	Medline	Web of Science
(u) Benign Fibro-Osseous Lesions of Periodontal Ligament Origin	Waldron et al., 1975 Neville and Albenesius, 1986	None
(v) Cementoma	MacDonald-Jankowski, 1992 Waldron et al., 1975 Loh and Yeo, 1989 Thompson and Altini, 1989 Lahbabi et al., 1998 Ogunsalu et al., 2001 Matzuzaka et al., 2002	MacDonald-Jankowski, 1992 MacDonald-Jankowski, 1996 Waldron et al., 1975 Kim and Lim, 1987 Thompson and Altini, 1989 Ogunsalu et al., 2001
(w) Osseous Dysplasia	MacDonald-Jankowski, 1992 Melrose et al., 1976 Waldron et al., 1975 Neville and Albenesius, 1986 Loh and Yeo, 1989 Swaroop et al., 1990 Lahbabi et al., 1998 Ogunsalu et al., 2001 Matzuzaka et al., 2002	MacDonald-Jankowski, 1992 MacDonald-Jankowski, 1996 Melrose et al., 1976 Waldron et al., 1975 Loh and Yeo, 1989

Both databases were last interrogated by all search terms on the 31st January 2003.

RESULTS

A: Radiology-only and histopathological-file-based cases of FCODs affecting the Hong Kong Chinese.

Radiology-only report.

Ten cases in the Hong Kong Chinese were identified and their records and radiographs reviewed; they are set out in Table 4.3. All cases were female. The mean age was 52.1 years. All cases were radiologically investigated either for pain from carious teeth or as part of a routine clinical assessment. Only one case (Case No. 7) exhibited swelling that could be due to expansion by the COD lesion of the buccal and lingual cortices of the mandible. The disposition of their lesions between jaws and sextants were displayed in Table 4.3. In declining order, the most common sites for the presence of these lesions were the posterior mandible, posterior maxilla, anterior mandible and anterior maxilla. The third stage (the complete radiopacity) was more frequently observed in the oldest women. Lesions in two Chinese women had been investigated histopathologically.

Histopathological-file-based report.

The clinical notes and radiographs and histopathological reports of 23 patients treated at the PPDH were reviewed; they were all female. The histopathological reports confirmed their FOL nature. The six solitary cases were

identified as Focal CODs and will be addressed separately. The details of the remaining 17 patients are set out in Table 4.4. The women had a mean age of 62.12 years (sd; 10.39 range 43 to 83). Twelve patients presented with symptoms arising from the lesions; the rest were incidentally observed on the radiological investigation prior to the provision of prostheses. There was a significant relationship between COD lesions and edentulous sextants ($X2 = 3.88$; 1df; $0.05 > P > 0.01$).

Twelve patients presented with bilateral lesions (mean age 62.7 years; sd 11.2) and five with unilateral lesions affecting both jaws (mean age 60.8 years; sd 6.6). They were all provisionally diagnosed as FCOD by the receiving clinician or the OMF surgeon.

B: Systematic Review

The search terms and both databases identified all but one report that may be relevant to the SR; Wu and Chan's report (1985) was only identified by reviewing the bibliographies. The Web of Science's 'cited reference search' did not identify any SR reports in addition to those already identified by the search terms and review of the bibliography. Table 4.1 displays each search term, the total number of reports, the recall and precision for both databases, and the identity of those reports.

Table 4.3. Florid Cemento-Osseous Dysplasia: Hong Kong Patients; Radiology Files

Case No.	Gender & Age (years)	Presenting Complaints	MANDIBLE			MAXILLA		
			Anterior	Posterior		Anterior	Posterior	
				Right	Left		Right	Left
1.	F 28	Incidental	Yes	No	No	Yes	Yes	Yes
2.	F 36	Incidental	Yes	Yes	Yes	No	No	No
3.[a]	F 43	Incidental	No	Yes	Yes	No	No	No
4.	F 46	Incidental	Yes	Yes	Yes	No	Yes	Yes
5.	F 48	Incidental	No	Yes	Yes	No	No	No
6.	F 52	Incidental	Yes	Yes	Yes	No	Yes	Yes
7.	F 59	Swelling	No	Yes	Yes	No	Yes	Yes
8.[a]	F 65	Incidental	Yes	Yes	Yes	Yes	Yes	Yes
9.	F 65	Incidental	Yes	Yes	Yes	Yes	Yes	Yes
10.	F 67	Incidental	No	Yes	Yes	Yes	No	No
Total			6	9	9	4	6	6

Abbreviation and Note: [a], investigated histopathologically.

Table 4.4. Florid Cemento-Osseous Dysplasia: Hong Kong Patients; Pathological Files

Case No.	Gender & Age (years)	Presenting Complaint	MANDIBLE			MAXILLA		
			Anterior	Posterior		Anterior	Posterior	
				Right	Left		Right	Left
Bilateral								
1.	F 43	Pain	Yes	Yes	Yes	No	No	No
2.	F 43	Incidental	No	Yes	Yes	No	No	No
3.	F 55	Pain	Yes	Yes *Edent*	Yes	Yes	Yes	Yes
4.	F 59	Pain.Swell	Yes *Edent*	Yes *Edent*	Yes *Edent*	No *Edent*	Yes *Edent*	Yes *Edent*
5.	F 60	Pain	No	Yes	Yes	No	No	No
6.	F 65	Incidental	Yes	Yes	Yes	Yes	Yes *Edent*	Yes *Edent*
7.	F 65	Incidental	No	Yes	Yes	No	No	No
8.	F 67	Pain.Swell	No *Edent*	Yes *Edent*	No *Edent*	No *Edent*	Yes *Edent*	Yes *Edent*
9.	F 68	Pain.Disch	Yes	Yes	Yes	Yes	Yes *Edent*	Yes *Edent*
10.	F 71	Pain.Swell	No	Yes	Yes	No	No	No
11.	F 73	Pain	Yes	Yes *Edent*	Yes	Yes	Yes	No
12.	F 83	Pain.Swell	No	Yes *Edent*	Yes	No	Yes	Yes
Unilateral								
1.	F 54	Pain	No	Yes	No	No	Yes	No
2.	F 54	Pain	No	Yes	No	No	Yes	No
3.	F 59	Discharge	No	Yes *Edent*	No *Edent*	No	Yes *Edent*	No *Edent*
4.	F 68	Incidental	Yes	Yes	No	No	Yes *Edent*	No
5.	F 69	Incidental	No	Yes *Edent*	No *Edent*	No	Yes *Edent*	No *Edent*

Abbreviation: Edent, edentulous

Of the 23 search terms used in Table 4.1, 'Osseous Dysplasia' recalled the most SR-included reports overall for Medline, but it had a low precision, which for Medline and Web of Science was 2.2 and 3.4, respectively. 'Gigantiform Cementoma' had the highest precision for both databases.

It was noted that Latin-America was not represented, therefore, a search of LILACS was made using the following search terms 'Florid Cemento-osseous Dysplasia', 'Florid Osseous dysplasia', 'Osseous Dysplasia', 'Gigantiform Cementoma' and 'Periapical cemental Dysplasia'. No SR-includable reports were found.

Table 4.5. Florid Cemento-Osseous Dysplasia: Excluded reports

Selection Criterion	Report (1st author's surname and date of publication)	Gp.	Language of Publication
2	Kuyama et al. (2000)	O	English
1	Kawai et al. (1999)	O	English
A	Ackerman & Altini (1992)	A	English
1	Yoon et al. (1989)	O	English
3	Higuchi et al. (1988)	O	English
2	Wu & Chan (1985)	O	English
1	Fujisawa et al. (1983)	O	Japanese
A	Shear & Rachanis (1979)	A	English
1	Regezi et al. (1978)	W	English
2	Kawai et al. (1974)	O	English
3	Bhaskar (1968)	W	English
3	Hamner et al. (1968)	W	English
2	Laband & Leacock (1967a)	A	English
1	Zegarelli et al. (1964)	A	English
1	Fontaine (1954)	W	English

Abbreviations: A, African; O, Oriental; W, Western.

Selection Criteria.

Many of the reports were automatically rejected because they were single case reports or review articles. Those excluded under specific exclusion criteria are set out in Table 4.5. There was no significant difference between the proportions of English with non-English SR-excluded reports (Table 4.5.) with the SR-included reports (4.6.) for the 4 global groups; $X^2 = 2.20$; 3df; $P > 0.05$.

Criterion 1.

Six reports were excluded under 'Criterion 1.'The report by Zegarelli and co-authors (1964) was excluded because they did not fully understand that cementifying fibroma (or fibrocementoma as they called it), cementoblastoma and COD are separate lesions. The report by Kawai and co-authors (1999) was excluded because it was unable to separate their 'focal' from their 'multiplex' cases. Yoon and co-authors' report (1989) was excluded, as the description in each of the three cases of Gigantiform Cementoma' was strongly suggestive of FGC. The reports by Regezi and co-authors (1978) and by Fontaine (1954) were excluded because the lesions they reported were essentially focal COD or PCD. Suarez and co-authors' (2001) report was partly salvaged, because 80% were FCODs. Neville and Albenesius' (1986) report was rescued and included in the SR because the 9 non-FCODs out of their 29 cases were readily identifiable and excluded.

Criterion 2.

Four reports were excluded under 'Criterion 2.' Those reports that were unable to satisfy the likelihood that the complete jaws had been radiographed to ensure the diagnosis of FCOD, were excluded. The reports by Wu and Chan (1985) and Kuyama and co-authors (2000) made no reference to radiographs and were excluded. Waldron and co-authors (1975) had only 14 cases with full radiographs out of 38 cases in their pathology file. As these 14 cases could be identified, the report was partially rescued and included in the SR. Only one of Laband and Leacock's double reported study (1967 a &b) will appear in Table 4.5.

Criterion 3.

Three reports were excluded under 'Criterion 3.' This criterion excluded those reports, which were clearly not derived from a complete collection of cases of FCODs occurring in the reporters' caseload. Both Hamner and co-authors' (1968) and Bhaskar's (1968) reports were based (partly and wholly, respectively) on secondary referrals from military communities and were therefore not representative of a hospital-based patient community. The single case of Eversole and co-authors (1972) was included because it was derived from a series of FOL cases from the same community. Higuchi and co-authors' (1988) report was concerned with only those CODs associated with cysts in the mandible and therefore selected and thus excluded.

Criterion A.

Two sets of reports were considered under 'Criterion A.' MacDonald-Jankowski's (1992a and 1996a) Hong Kong Chinese reports displayed overlap, but the two double-reported Chinese cases (also the only histologically-confirmed were identified and removed from the earlier 1992 report in the SR, rendering it solely radiology-file based. Both reports were now admitted to the SR. Ackerman and Altini (1992) reported the classical cases already reported by Thompson and Altini (1989); the former was excluded. Shear and Rachanis' (1979) smaller report was included within Thompson and Altini's larger report and excluded.

The present study and the SR

Twenty reports of series of cases, including the present author's 3 series, were included in the SR (Table 4.6). There is no statistical difference for the proportion of English-language published reports for the 17 SR-included in Table 4.6; or the 15 excluded (Table 4.5); $X^2 = 0.57$; 1df; $P > 0.05$. A synthesis of the 18 SR-included reports is compared statistically to the present author's 2 Hong Kong series in Table 4.7. The distribution of the reports globally is set out in Map 4.1.

Two of the SR-included reports (MacDonald-Jankowski, 1992a; Neville and Albenesius, 1986) were wholly or substantially, not biopsied, derived from non-histopathology-file sources. Of the reports included in the SR, Medline recalled seven reports that were not recalled by Web of Science, whereas the latter recalled

one report (Kim and Lim, 1987) not found in the former. Although this report (Kim and Lim, 1987) was an abstract, it was published in a Medline-indexed journal. Nine search terms produced reports that were included in the SR for both databases. Medline provided SR-included reports for nine search terms for which the Web of Science gave none. Waldron and co-authors' (1975) report was the most cited, seven times each in Medline and the Web of Science. One report, that by Yoon and co-authors (1989), had not been recalled by any of the search terms for either database. It was instead discovered during the search for reports on FOLs in general.

In Table 4.6, the number of reports with available details varied from 16 for gender to 5 for the presence or absence of a fistula or of a discharge of pus in the cases of FCOD observed in 20 series of patients reported in 19 reports. Ninety-three (59%), 58 (37%; including Saini's (1991) Black Saudis) and 5 (3%) cases occurred in Black, Oriental and Caucasian patients (including three Indians) respectively; the race was unknown in 2 cases (Melrose et al., 1976; Lahbabi et al., 1998). The specific ethnic origin of the Orientals was clear in 8 reports; 4 in Japan (Sakato, 1976a; Tanaka et al., 1987; Miyamoto, 1996; Matsuzaka et al., 2002), 2 in China, (MacDonald-Jankowski, 1992a and 1996a) and one report each for Singapore (Loh and Yeo, 1989) and Korea (Kim and Lim, 1987). Ninety-seven percent of the 153 cases that identified gender were female. Both the radiology-only and histopathology-file-based Hong Kong reports displayed no significant gender-differences in comparison to the rest of the SR ($X^2 = 0.33$ and 0.7 respectively: 1df: $P > 0.05$). Furthermore, there was no

significant difference between Oriental and the other reports ($X^2 = 0.05$; 1df; $P > 0.05$)

The mean age for 101 cases was 49 years. Although a mean age of 47 years was observed in three (Tanaka et al., 1987; Loh and Yeo, 1989; MacDonald-Jankowski, 1992a) of four Oriental series, the oldest mean age in the SR was for the Hong Kong Chinese series derived from histopathological files (a mean of 62 years; MacDonald-Jankowski , 1996a). This was significantly older than the radiology-only series (MacDonald-Jankowski, 1992a) for the same dental hospital patient community over a similar period ($t = 3.06$; 23df; $0.01 > P > 0.001$). As reported by Neville and Albenesius (1986), the only other report that was largely based on radiology-only report only diagnosis did not include a mean age, so observation of a similar phenomenon between comparable non-Oriental communities was not possible.).

The radiology-only Hong Kong report has significantly few cases of swelling than the histopathological-file-based report; $X^2 = 9.11$; 1df: $P < 0.001$. Neither the radiology-only nor the histopathology-file-based Hong Kong reports differed from the rest of the non-Hong Kong SR with regards to swellings ($X^2 = 0.84$ and 0.12 respectively; 1df; $P > 0.05$). The radiology-only Hong Kong report has significantly few cases of swelling than the histopathological-file-based report; $X^2 = 9.11$; 1df: $P < 0.001$.

Table 4.6. Florid Cemento-Osseous Dysplasia: Systematic review; Analysis of the included reports

First Author (year)	National and/or Ethnic origin (Number of Hospitals(H) and number of Cities(C))	**Period covered**	Number of FCODs (No. per hospital per yr)	**Gender** Male Female	Age **mean** (range) in years / *Pre-presenting duration* ***mean*** *(range) in years*	**Presenting Signs and Symptoms** (percent) Swelling	Pain	Other	**SITE** Mandible Ant.	Mandible Post.	Maxilla Ant.	Maxilla Post.	**Histopathology**	**Comments**
Eversole (1972)	US (1B)	ING	1	0 1	**71** / *ING*	ING	ING	ING	1		1		1	Part of a FOL series
Waldron (1975)	US(12B:2 W) (1H:1C)	17 years	14(0.82)	0 14	ING(34-67) / *ING*	4	8	3Incid 5DisP	IIG		IIG		38 Only 14 had full radiography	
Melrose (1976)	US(32B:1O:1 ?) (1H:1C)	ING	34	1 33	**42**(26-59) / *ING*	16	9	23Incid	32(34)34		22(24)22		48 Only 34 included full radiography	7 max. & 20 mand. Had symmetrical distribution
Sakato (1977)	Japanese (1H:1C)	ING	9	1 8	IIG / *ING*	ING	ING	ING	9		5		9	Excluded 5 Familial cases
Neville (1986)	US (20B) (1H:1C)	4 years	20(5.0)	0 20	ING(21>80) / *ING*	ING	ING	ING	IIG		IIG		8	Some of the 9cases excluded may be PCD, 8 biopsied
Kim (1987)	Korean (1H:1C)	20 years	1(0.05)	ING	ING / *ING*	ING	ING	ING	ING		ING		All 50 cemental lesions	3 cases of PCD in anterior mandible
Tanaka (1987)	Japanese (1H:1C)	ING	3	0 3	**47**(34-65) / *ING*	0	0	3Incid	3 2	3	3 1	3	3	Included other 26 Japanese cases
Loh (1989)	Singaporean (8Chin:1In) (1H:1C)	31 years	9(0.3)	0 9	**47**(37-59) / *ING*	4	9	9DisP &seq.	9		5		9	All affected jaws affected bilaterally
Thompson (1989)	South African (8B) (1H:1C)	1964-1984 20 years	8(0.4)	0 8	**56**(39-74) / *ING*	IIG	IIG	IIG	8 2	8	6 0	6	8	

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Gender Male Female	Age	Swelling	Pain	Other	Mandible Ant.	Mandible Post.	Maxilla Ant.	Maxilla Post.	Histopathology	Comments
Swaroop (1990)	Indian (1H:1C)	1963-1981 18 years	2(0.1)	ING	ING	ING	ING	ING	ING		ING		2	
					ING									
Saini (1991)	Saudi Blacks (1H:1C)	ING	4	0 4	**43**(38-48)	1	ING	3Incid	IIG		IIG		4	Poor quality figure
MacDonald (1992)	British (6) (1H:1C)	1988-1990 2 years	6(3.0)	0 6	**54**(37-67)	0	0	6Incid	6		6		Radiographs only	5 max. & 5 mand. had symmetrical distributions
					0				4	6	2	6		
MacDonald (1992)	Chinese (1H:1C)	1982-1992 10 years	8a(0.8)	0 8	**47**(28-65)*	1	ING	7Incid	8		5		Radiographs only	* 2 other cases included in 1996. 5 max. & 7 mand. Had symmetrical distributions
					0				6	7	3	5		
Groot (1996)	Dutch (5B) (1H:1C)	ING	5	0 5	**53**(33-66)	3	5	5 fistu	5		6		IIG	
					ING			0Incid	0	5	0	3		
MacDonald (1996)	Chinese (1H:1C)	10 years	17(1.7)	0 17	**62**(43-83)	4	11	5Incid 1DisP	17		12		17	5 max. & 11 mand. had symmetrical distributions
					ING				7	17	4	12		
Miyamoto (1996)	Japanese (1H:1C)	20 years	13(0.6)	IIG	ING	ING	ING	ING	ING		ING		13	
					ING									
Lahbabi (1998)	French (4B:1?) (1H:1C)	ING	5	1 4	**46**(33-64)	0	3	2Incid	6		1		5 pans & 1 CT	Text & figures not so clear on maxillary lesions
					ING				3	5	0	1		
Ogunsalu (2001)	Jamaican (2H:2C)	1980-1995 15 years	2(0.13)	0 2	**48**(47-49)	ING	ING	ING	2		0		2	Excluding 1 GC-had only 1 lesion Also had 1 PCD
					ING				0	2				
Suarez (2001)	US (2H:1C)*	ING	19	IIG	IIG	IIG	IIG	IIG	19		19		19	*95% of 24 cases are Black
					ING									
Matsuzaka (2002)	Japanese 1C;1H)	1966-2001 35 years	7(0.2)	2 5	IIG(30s-60s)	ING	ING	ING	IIG		IIG		7	
					ING									

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Gender Male Female	Age	Swelling Pain Other			Mandible Ant. Post.	Maxilla Ant. Post.	Histopathology	Comments
Mean					49[c](21-83) *0*[d]							
Total number of FCOD cases			187	5[b] 147[b]		33[e]	45[f]	Incid 52[g] Pus 24[h]	126/126 56[k] 87[k]	90/126 32[k] 58[k]		
% of total number				3 97		27%	40%	42%[g] 53%[h]	100%	71%		
Number of reported series			(12)[a]	16	12 (12) *0(0)*	10	8	10	13	13		
% of total 20 series			(60)	80	60 (60) *0(0)*	50	40	50	65	65		

Abbreviations and Notes: GC, gigantiform cementoma; Mand, mandible; Max, maxilla; PCD, periapical cemental dysplasia.

Key	Number of reports	Total number of cases
a.No.FCOD/H/Yr	12	101
b. Gender	16	152
c. Mean Age	12	101
d. Awareness	0	0
e Swelling	10	125
f Pain	8	113
g Incidental	10	125
h. Pus/Discharge	4	45
i. Site:Mandible	13	126
j. Site:Maxilla	13	126
k. Site:Ant./Post	9	88
l. Follow-up/ Recurrence	0	0

Map 1.

In addition to the observation that the histopathological-file-based Hong Kong report reported significantly more cases of pain than the non-Hong Kong SR, the Oriental reports presented with significantly more pain than those reported than the rest of the SR ($X^2 = 14.00$; 1df: $P < 0.001$).

Less than half of 125 cases were discovered incidentally to an investigation of a separate complaint. Those cases of the radiology-only Hong Kong report were significantly more frequently found incidentally in comparison to the rest of the SR ($X^2 = 6.72$; 1df; $0.01 > P > 0.001$), whereas those of the histopathology-file-based report displayed no significant difference ($X^2 = 0.57$:1df: $P > 0.05$). The radiology-only report's greater association with incidental finding was significantly greater than that for the pathology-file-based report ($X^2 = 7.51$; 1df: $P > 0.05$).

Both the radiology-only and the histopathology-file-based reports were combined and compared with the rest of the SR in Table 4.7. The frequencies of FCODs found as an incidental finding or associated with pain and swelling in the Hong Kong Chinese were not significantly different to those in the rest of the SR (largely Black people).

Table 4.7. Florid Cemento-Osseous Dysplasia: Chi-square statistics

Feature	Hong Kong*	Rest of SR	X^2	Deg. free	P
Gender:Male:Female	0:25	5:122	0.98	1	> 0.05
Swelling:Yes:No	5:20	28:72	0.66	1	> 0.05
Pain: Yes:No	11;6	34:60	5.10	1	0.05 > P > 0.01
Incident.Find:Yes:No	12:13	40:60	0.53	1	> 0.05

Abbreviations: * combined 8 cases from the radiology-only and 17 from the histopathology-file series; Incident.Find, incidental finding; Dg.Fre, degrees of freedom; SR, systematic review.

The mandible was involved in all and the maxilla in two-thirds of 97 cases. The frequency with which anterior and posterior areas were affected was 99%, 73%, 64% and 36% for the posterior mandible, posterior maxilla, anterior mandible and anterior maxilla, respectively. There was no difference between Oriental and other series with regards to the frequency that the maxilla or the anterior areas of the maxilla and mandible were affected.

Symmetry with regards to the sextants affected, rather than mirror image symmetry *per se*, was an important feature of FCOD whenever assessable. Symmetry was assessable in three reports and appeared to be greatest in the Chinese series, although in the histopathology-file-based report (MacDonald-Jankowski, 1996a) five lesions were completely unilateral in distribution. The ratio of the symmetrical maxillary to mandibular lesions was greater in one of the radiology-only reports (MacDonald-Jankowski, 1992a). This may reflect the fact that the symmetrically disposed COD lesions allowed the clinicians to confidently diagnosis these FCODs solely on their radiology without the need for biopsy.

DISCUSSION

In this study, the Medline database produced more useful reports than the Web of Science. As a central aim of a SR is to "systematically search... the world literature on a specific issue" (Sackett et al., 2000), then a literature search by the Web of Science should be supplemented by a medical database such as Medline.

Generally, searches are a combination of MeSH (in Medline) and free-text search terms. The only relevant MeSH term was 'Cementoma', first used as such in 1971. Although its definition in its 'scope note' would not be inconsistent with that of 'Cementoma' in the first edition of the WHO's classification of odontogenic tumours (Pindborg et al., 1971), it did not include any of the WHO's subclassification of 'cemental' lesions as 'entry terms' (alternative nomenclature or subclassified lesions). Furthermore, when 'Cementoma' was used as a search term in a free-text search it did not identify any useful references not identified by other search terms. This highlighted both the limitations of the current MeSH in some areas of health care such as dentistry and radiology, and the importance of free-text searching. The latter was enhanced if the terms appear in the title or abstract of papers submitted for indexing, because free-text searching was an automatic direct electronic search of all titles and abstracts in the database. The report by Wu and Chan (1985) was not identified by either database search because none of the search terms appeared in either their report's title or abstract.

The most effective search terms in terms of both recall and precision were 'Florid Osseous Dysplasia' and 'Gigantiform Cementoma'. Although recall and precision are central properties of database searching, recall generally takes precedence, particularly in SRs in which the principal aim is to acquire the largest number of relevant papers. Although it was not unexpected that the most non-specific terms such as 'Cementoma' and 'Osseous Dysplasia' would have the highest recalls, certainly for Medline (which used 'Cementoma' as a MeSH), it was unexpected that 'Osseous Dysplasia' would be so effective, as it has not been used

with respect to FCOD for decades. Therefore, as it is not possible to determine the efficiency of a search term in advance, the use of a wide range of nomenclature as search terms was justified.

Over time, as it became clear that conditions labelled 'Chronic Sclerosing Osteomyelitis' were not associated with infection, leading to the development of 'Cementoma' and 'Benign Periapical Fibroma'. There were those, such as Robinson (1956), who still proposed a reactive cause for these lesions, calling this lesion 'Osseous Dysplasia'. Waldron and co-authors (1975) advocated a periodontal ligament origin for this group of lesions because this class of lesion was generally confined to the alveolus and contained a histopathological appearance similar to that seen in the normal periodontal ligament. This concept is still acknowledged by many authorities (Brannon and Fowler, 2001; Slootweg, 2005), although Kawai and co-authors (1999) disapprove; their reasoning was discussed in Chapter 1.

Although Waldron (1985) considered that the majority of cases called 'Chronic Sclerosing Osteomyelitis' were 'Florid Osseous Dysplasia' (FOD), Panders and Hadders (1970) used 'Chronic Sclerosing Osteomyelitis' in relation to cases that were clearly similar to Groot and co-authors' (1996) 'Diffuse Sclerosing Osteomyelitis', differing markedly from 'Florid Osseous Dysplasia'. The former affected the basal process of the mandible in addition to the alveolar process, to which the latter was largely confined. SR reports identified by 'Diffuse Sclerosing Osteomyelitis' included this term in the title (Groot et al., 1996) or abstract (Tanaka et al., 1987; Lahbabi et al., 1998) as a lesion other than FCOD. Although 'Chronic

Sclerosing Osteomyelitis' and the more general 'Sclerosing Osteomyelitis' identified many reports, very few were SR-included reports. 'Enostosis' is now used as a synonym for idiopathic osteosclerosis (also known as 'dense bone islands') that do not need treatment (Greenspan, 1995).

WHO's second edition terminology of FCOD published in 1992 has not been consistently applied subsequently (Kramer et al., 1992). Not only has the older "Florid Osseous Dysplasia" and even the almost obsolete "Gigantiform Cememtoma" recalled more SR-included reports on both databases, the latter identified two published in the last 2 years; these were not identified by the search term "Florid Cemento-Osseous Dysplasia". Although this can be expected as older terms will be more familiar, another reason could be that many authors may have considered the hyphenated 'Cemento-Osseous' unnecessary, for which they have some justification. The term 'Cemento-Osseous Dysplasia' is a histopathological term rather than a clinical or radiological term, yet diagnosis of FCOD is decided by clinical and radiographic investigation, its histopathology being similar to the two other FOLs; COF and FD.

Even before WHO's second edition expanded its definition of PCD to include cases with lesions in posterior areas, it had already been used as a synonym for FCOD. Of the 20 SR-included reports, 2 used PCD to describe lesions that were consistent with FCOD (Neville and Albenesius, 1986; Tanaka et al., 1987), and one mentioned PCD in the abstract but FCOD in the body of the text. (Miyamoto, 1996)

Although the SR has shown that identification and application of the varied nomenclature of FCOD has been valuable for recalling reports from databases, it cannot do more than indicate which terms are most useful for such a purpose.

Nevertheless, it is clear from the titles and abstracts of recent papers that some of the terms such as 'Florid Osseous Dysplasia' that were in vogue before the recommendations of the WHO's second edition are still being used. The continued use of many of those should not cause confusion, provided that they have not already become associated with other specific lesions, such as 'Periapical Cemental Dysplasia' and its variant names, 'Sclerosing Osteitis' and 'Sclerosing Osteomyelitis'. Special care is needed using the term 'Familial Multiple Cementomas' (the other WHO's second edition FCOD synonym; Kramer et al., 1992). This term recalled two reports of FGC, which has a different clinical presentation and prognosis (Waldron, 1993). Most cases of FGC have been reported in Caucasian kindreds, affecting all age groups of both genders equally. Also, the behaviour of many of the lesions are more akin to neoplasia, exhibiting progressive growth and necessitating surgery, which was otherwise contraindicated for the largely asymptomatic conventional form.

Stypulkowska and co-authors' (1998) report on 40 years coverage of oral tumours in a European community, which clearly considered FCOD, did not reveal a single case of FCOD, supporting the outcome of the SR that FCOD occurs more frequently in patients of Black African and Oriental origin than in Caucasians.

It is clear from Map 1 that almost all non-Black-based reports are Oriental; Swaroop and co-authors' (1990) Indian report, is the only Caucasian community reported so far. Therefore, the question considers more specifically whether the presentation in Orientals varies significantly from that in those of Black African origin.

Although series of FCOD in Oriental communities are just as frequently reported as those in Black communities, the former's very low 'number of FCOD cases per hospital per year' values in comparison with those of the latter's would indicate that the frequency of FCOD in Orientals may be lower than that experienced in Black patients. This phenomenon was more clearly seen in a report in which diagnosis was primarily radiological; the 'number of FCOD per hospital per year' in a Black British series was particularly high in comparison with a Hong Kong Chinese series (MacDonald-Jankowski, 1992a). The 'number of FCOD per hospital per year' in the last series was half that observed in the same author's Chinese histopathology-file-based report. This can be explained by reports derived from histopathology files being dependent upon the presence of clear indications for the surgery that is required to produce the pathological specimen. Such indications may only be forthcoming in a fraction of cases, as most may be symptom-free. Nevertheless, it is those symptomatic cases that compel the patient to seek treatment and ultimately appear in the histopathology file. Some support for this contention was revealed in the SR. MacDonald-Jankowski's (1996a) histopathology-file-based report was associated with symptoms. This series not only had the oldest mean age, but it is significantly older in comparison with the series from the radiology-only

report (MacDonald-Jankowski, 1992a) in the same community, in which nearly all FCODs were observed as symptom-free and incidental findings on radiographs taken to investigate other complaints.

An important finding in the histopathology-file-based Chinese report was a significant association between edentulous areas and COD lesions, which could contribute a secondary infection and therefore symptoms (MacDonald-Jankowski, 1992a). The report by Loh and Yeo (1989) most clearly displays the association between pain and discharge of pus and sequestrae formation. Furthermore, Waldron and co-authors (1975) claimed that most of their symptomatic cases had been "edentulous in the affected areas for many years"; all their 10 biopsies from edentulous sites had symptoms, whereas the four from dentate areas had none. Therefore, a significantly higher prevalence of pain in Oriental, mainly Chinese, reports may reflect this association between these lesions and edentulous areas. Otherwise, the essential character of FCOD is to remain symptom-free unless secondarily infected.

Symmetry of distribution was an important observation. In the radiology-only report, it appeared that symmetry of distribution within both the maxilla and the mandible was a feature of the Hong Kong Chinese, (MacDonald-Jankowski, 1992a) but when compared with the histopathology-file-based report (MacDonald-Jankowski, 1996a) on patients from this community this feature is less evident. The ratio of symmetry of maxillary lesions to mandibular lesions is also greater in the radiology-only report (MacDonald-Jankowski, 1992a), whereas the Hong Kong

histopathology-file-based report (MacDonald-Jankowski, 1996a) was comparable with the lower symmetry reported by Melrose and co-authors (1976) which was also a histopathology-file-based report. Furthermore, in the Hong Kong histopathology-file-based report (MacDonald-Jankowski, 1996a) the unilateral, and therefore asymmetrical, cases were on average younger than the bilateral cases. This unilateral presentation in younger patients may represent a transition stage to the classical bilateral distribution of the more mature lesion. It is most likely that the greater bimaxillary and symmetrical presentation of the radiology-only report allowed them to be diagnosed confidently as FCOD, whereas those cases not exhibiting this presentation were biopsied and entered the histopathology-file-based series.

CONCLUSIONS

1. As a response to the PICO question, there does not appear to be an alternative to multi-quadrant radiology. But this should not be a significant disadvantage, in terms of radiation dose to the patient, if it is clearly clinically indicated. Furthermore, a single panoramic radiograph can be sufficient to achieve this. Diagnosis of a FCOD could be confidently made on the involvement of more than one sextant on a panoramic radiograph, which need not be bimaxillary or symmetrical.

2. The two at risk global communities appear to be Black African and Oriental.

3., Other than a significantly lower prevalence of pain in the Hong Kong Chinese, there did not appear to be other differences in presentation between this

community and that rest of the SR. The clinical presentation obviously varies with the source of the case series; those from histopathological files are more likely to present with symptoms whereas those from radiology-only reports are more likely to be detected as incidental findings and are symptomless.

4. The most effective search terms are 'Florid Osseous dysplasia'; and 'Gigantiform Cementoma', whereas those with the greatest recall are 'Cementoma' and 'Osseous Dysplasia'.

5. As the maturation progress of FCOD has not been established, a longitudinal review of FCOD cases could determine their progress and sequelae, particularly with regard to edentulous areas. A better understanding of these could enhance dental management of increasingly ageing populations, particularly in the West (where the majority of reports regarding Black patients originate) and in the Orient.

6. The mean age of a particular community may depend on whether it was a histopathology-based or a radiology-only study, as symptoms-free lesions observed as incidental findings on radiographs were younger than those with presenting symptoms.

Chapter 5.

FOCAL CEMENTO-OSSEOUS DYSPLASIA

INTRODUCTION

Since the publication of the second edition, the 'Focal Cemento-Osseous Dysplasia', has been recognized as form of COD. Earlier Waldron (1985) observing its localized nature first reported it as the 'localized fibro-osseous-cemental lesion', which Summerlin and Tomich (1994) renamed as 'focal cemento-osseous dysplasia' (FocCOD). They further characterized its salient features and compared them to those of the COF, the FOL most likely to feature on its differential diagnosis.

Summerlin and Tomich (1994) considered whether FocCOD was a new entity. They believed that it has been reported as a COF, citing their own experience of discovering FocCODs when they reviewed their own cases of COFs. A similar experience was reported by Su and co-authors (1997a and b). Unfortunately, neither disclosed how many were misdiagnosed. This is an important point, because it could add another factor; namely that some COFs or FocCODs may have been actively considered as other lesions and excluded. Although it is likely that this would have been done, it was decided not to make this an issue in this SR provided that reports (considered for inclusion) also reported COFs; such reports would be those published before Summerlin and Tomich (1994). Furthermore, they all should cite at least WHO's first edition (Pindborg et al., 1971) and/ or Waldron and co-authors' (1975)

report and thus be aware of the importance of distinguishing COFs from FocCODs. For those published subsequently, it was sufficient that they merely cite Summerlin and Tomich (1994) to earn the rebuttable presumption that they adhered to Summerlin and Tomich's (1994) criteria, particularly those pertaining to appearance at surgery and gross presentation of specimen. These centrally important criteria were reiterated by Melrose (1997).

This study considered only the focal forms of COD that occurred in a series in the reporting authors' caseload, thereby excluding case reports. This form could occur in any area of the alveolar process either as a solitary (single) lesion or a group of juxtaposed lesions within a sextant.

AIMS AND RESEARCH QUESTIONS

The primary research question for this SR, or PICO question, is: -"Do other clinical and radiological features improve diagnosis of FocCOD compared with a localized FOL which is not readily 'shelled-out' during enucleation, presenting a fragmented specimen?"

In order to answer this question only those reports that did not contradict the essential definition of a FocCOD (A fragmented surgical specimen which is histologically confirmed as a FOL.) can be admitted to this SR. In addition to this question there are other supplemental questions, which help to frame the selection criteria for the above PICO question; these are: -

Question 1: What are the clinical and radiological characteristics observed in a largely Southern Chinese Hong Kong community?

This requires a detailed analysis of the clinical and radiological features observed in a continuous series of cases of FocCOD lesions in a Hong Kong Chinese community admitted to PPDH.

Question 2: Do the Hong Kong Chinese/Oriental communities have a different presentation of FocCOD compared with non-Chinese/Oriental communities?

Comparison of the Hong Kong Chinese with the rest of the SR will be addressed in this chapter. Comparison of the Oriental communities with regards to other global communities will be addressed in Chapter 8. To assist the formulation of an answer the SR-included reports will be divided into four global groups, Western, African, Oriental and Latin-American, broadly reflecting ethnic origin.

MATERIAL AND METHODS

A: The histological file-based FocCOD

Cases were searched for in the histopathology files of PPDH under the following terms; PCD, GC, FOD, FCOD and sclerosing osteomyelitis. Panoramic radiographs were available in all cases, and periapical and occlusal radiographs for some. The radiographs were reviewed on standard viewing boxes sited in reduced ambient lighting.

B: Systematic Review.

A SR is required to answer the PICO question. A SR requires not only a literature to search, but also selection criteria to sift this literature. As the primary aim is to include as many reports as possible a wide search of the literature will be made, including non-English reports.

Selection criteria.

Inclusion criteria.

There were 3 inclusion (Criteria 1 to 3) and 1 exclusion (Criterion A) criteria for the SR. Each report will pass through these criteria in strict sequence. Although a report may be excluded by more than one criterion, only the first criterion to exclude a particular report will appear in Table 5.3. [For the sake of brevity only those reports which cannot be readily identified from their title or abstract will be discussed and cited.]

'Exclusion' refers to the 'non-inclusion' of a report within the SR and will be used regardless of whether it is in relation to either 'inclusion' or 'exclusion' selection criteria.

Criterion 1. The study should be consistent with the WHO definition of FocCOD.

The study must be consistent with the WHO definition of FocCOD by either of the two pathways for inclusion out-lined in the introduction; Summerlin and Tomich's (1994) clinical and radiological criteria of such lesions whose histopathology was consistent with the WHO's definition of COD, or cite at least the WHO's first edition (Pindborg et al., 1971) and or Waldron and co-authors (1975) and include a report on COFs. The histopathology must be that of an FOL. The specimen at time of surgery should not be easy to 'shell-out'; suggestions within a report to the contrary would lead to its exclusion.

Criterion 2. FocCOD rather than FCOD, which is classically described as bilateral.

As it is necessarily to exclude cases of FCOD, complete radiography is required of the whole jaws. If a report contains a number of cases that have not had complete radiography of their jaws and cannot be identified and excluded, then the whole report can enter the SR provided that these cases do not exceed 10% of the report.

FocCOD has been widely understood as a solitary lesion or a single group of juxtaposed lesions affecting a single sextant. Although it is not always clear whether the reports have reviewed each patient to ensure this lesion is truly focal, as just described, it is presumed that for these recent reports that the ubiquitous availability of panoramic radiography would have addressed this issue. This presumption is

rebuttable and all reports are scrutinized for any inconsistency in this regard. It is anticipated that an author may consider a case presenting with CODs affecting both jaws on one side or 2 adjacent sextants to represent FocCODs. Such a report including the latter can be included if such cases do not represent more than 10% of the report.

Furthermore, although hypercementosis was expressly excluded from the definition for FocCOD, Kawai and co-authors (1999) reported this as one of the manifestations of COD, and challenges the now established view that CODs are wholly osteogenic. Nevertheless, because this SR is concerned with solitary lesions, it is important to uphold this criterion to ensure consistency.

Criterion 3. The study should represent a complete collection of cases of FocCOD occurring in the reporters' caseload.

The study should represent a complete collection of cases of COF, arising within a particular community, occurring in the reporters' caseload. Reports that were merely a selection of cases such as case reports and those studies, which were primarily concerned with specific investigations or a discrete age group, such as children or a particular jaw, were excluded.

Exclusion Criteria

The literature consistent with the above inclusion criteria was then subjected to more specific exclusion criteria:

Criterion A. Excluded reports whose data have already been reported and included in the review.

Generally the largest and most detailed reports will be chosen over the lesser.

Databases

The PubMed interface of Medline and LILACS were interrogated by the following search terms focal or localized or solitary cemento-osseous or osseous dysplasia and periapical cemental dysplasia. This search was supplemented by a hand-search of those journals listed in Table 3.1. This strategy was further augmented by reference-harvesting of the bibliographies of all reports identified by the databases or hand-searching.

Definition of parameters.

The number of years is calculated on the assumption the study begins on the January of the beginning year and ends on the December of the closing year unless stated otherwise in the text.

The 'number of FocCODs per hospital per year' reflected the number of hospitals contributing to the report and the number of years from which the reported series was derived.

The jaws were further divided into posterior (molar and premolar) and anterior (incisors and canines) sextants. Although the demarcation point between these areas was infrequently expressed, it was taken to occur at a vertical line just distal to the distal surface of the canine.

The lower border of the mandibular alveolus is set by the inferior dental (mandibular) canal and the upper border of the maxillary alveolus on panoramic radiographs is set by the image of the hard palate on panoramic radiographs or lateral cephalographs (MacDonald-Jankowski, 2004a).

Significant differences in frequencies were tested by the X^2 test with $P < 0.05$. Significant differences in age were tested by a Student' t-test with $P < 0.05$.

RESULTS

A: Histopathological-file-based Hong Kong study

Table 5.1 displays the 6 solitary COD lesions (diagnosed in the 10 years between January 1982 and June 1992) were all observed at least on the panoramic

radiographs. All were female. Their mean age was 53.5 years (sd 9.40; range 42 to 65). All affected edentulous areas of the posterior mandibular alveolus. Three presented with pain and 2 as incidental findings. Their provisional diagnoses are found on Table 5.2. Three were identified solely as 'cementomas'.

'Cementoblastoma' was considered in two cases.

Their radiology is summarized in Table 5.5. All were well-defined. None displayed root resorption or tooth displacement.

B: Systematic review

Selection Criteria.

Many of the reports were automatically rejected because they were single case reports or review articles. Those excluded under specific exclusion criteria are set out in Table 5.3. There was no significant difference between the proportions of English with non-English SR-excluded reports (Table 5.3) with the SR-included reports (5.4) for the 4 global groups; $X^2 = 0.13$; 3df; $P > 0.05$.

Table 5.1. Focal Cemento-Osseous Dysplasia; Hong Kong Patients; Pathological Files.

Case No.	Gender & Age(years)	Presenting Complaint	MANDIBLE			MAXILLA		
			Anterior	Posterior		Anterior	Posterior	
				Right	left		Right	left
Solitary								
1.	F 37	Numb	No	Yes *Edent*	No	No	No	No
2.	F 42	Pain	No	Yes *Edent*	No	No	No	No
3.	F 45	Incidental	No	Yes *Edent*	No	No	No	No
4.	F 60	Pain	No	Yes *Edent*	No	No	No	No
5.	F 60	Incidental	No	No	Yes *Edent*	No	No *Edent*	No
6.	F 65	Pain	No	No	Yes *Edent*	No	No	No

Abbreviation: Edent, edentulous

Table 5.2. Focal Cemento-Osseous Dysplasia; Hong Kong Patients; Differential Diagnosis

Case No.	Gender & Age(years)	Differential or Provisional Diagnosis					
		Cementoma	Cementoblastoma	Odontoma	Osteoma	Calcifying odontogenic .cyst	Osteomyelitis
1.	F 37		1				1
2.	F 42			1	1	1	
3.	F 45	1					
4.	F 60	1					
5.	F 60	1					
6.	F 65	1	1		1		

Table 5.3. Focal Cemento-Osseous Dysplasia: Excluded reports

Selection Criterion	Report (1st author's surname and date of publication)	Gp.	Language of Publication
3	Ogunsalu et al. (2001)	A	English
3	Suarez et al. (2001)	W	English
1	Kawai et al. (1999)	O	English
2	Wu & Chan (1985)	O	English
1	Regezi et al. (1978)	W	English
3	Waldron et al. (1975)	W	English
3	Kawai et al. (1974)	O	English
3	Bhaskar (1968)	W	English
1	Hamner et al. (1968)	W	English
1	Zegarelli et al. (1964)	A	English

Abbreviations: A, African; O, Oriental; W, Western.

Criterion 1

Four reports were excluded under 'Criterion 1.' Zegarelli and co-authors (1964) did not fully understand that cementifying fibroma (or fibrocementoma as they called it), cementoblastoma and COD are separate lesions; Hamner et al. (1968) included many COFs; Regezi et al. (1978) must have included an indeterminate number of COFs among their PCDs. The report by Kawai et al. (1999) was excluded because very few cases had been examined histopathologically. The SR included reports by Eversole and co-authors (1972), Sakota (1977b), Slootweg and Muller (1990), Ackermann and Altini (1992), which did not cite Summerlin and Tomich (1994), because they were published earlier. They were included because they were consistent with the alternative pathway set out in the introduction. Although the more recent report by Matsuzaka and co-authors (2002) did not cite Summerlin and

Tomich (1994), it was clear from the detail of their report that their 'PCDs' were FocCODs. Ackermann and Altini (1992) also applied the term 'Gigantiform Cementoma' to their lesions, of which 59% were clearly single lesions and included in the SR, whereas the rest were excluded.

Criterion 2.

One report was excluded under 'Criterion 2.' Wu and Chan's (1985) report, made no reference to radiographs. Their report would also have been excluded under 'Criterion 3' because their PCDs, according to the WHO's first edition clearly considered only lesions localized to the anterior mandible, and thus under-reported FocCODs. In addition to the 19 cases already SR-included, Eversole and co-authors (1972a) also reported 35 other FOLs, which could have been FocCODs, but they were readily excluded because they were not accompanied by radiographs.

Although Summerlin and Tomich (1994) established the FocCOD as a clear clinical entity, they had radiographs only for 120 of their cases; these were the only cases included in the SR. The rest would appear to have been determined to be FocCODs by other criteria and were excluded. Sakota (1977b) reported 16 lesions in 14 patients, but because this report was dedicated to solitary FOLs (He provided another report dedicated expressly to multiple lesions.) it was presumed that the extra lesions were juxtaposed and compatible with the definition of FocCOD; this report was admitted. Ohkura (2001; cited Summerlin and Tomich; 1996) also reported cases of which 2 affected both jaws; this report was admitted because these cases

accounted for less than 10% of the report. Radiographs (both diagnostic and follow-up) were available to Miyamoto (1996); it was assumed that that only those lesions that were consistent with Summerlin and Tomich's (1994) criteria were admitted to his report.

Criterion 3.

Five were excluded under 'Criterion 3'. Not included were those reports clearly not derived from a complete collection of cases of FocCODs occurring in the reporters' caseload. Although Ogunsalu and co-authors (2001) recently included among their FOLs 2 lesions, which would qualify as FocCODs, their lack of awareness of FocCOD suggested that this lesion was underreported. Suarez and co-authors' (2001) reported 5 non-multicentric lesions that they termed 'periapical CODs"; because no further information about these was given they were excluded.

Waldron and co-authors (1975) selected only those lesions, which presented radiographically as "uniformly dense sclerotic mass(ses) at least 1.5 cm in diameter..." and also they expressly excluded typical PCDs. They were excluded.

The present study and the SR

There is no statistical difference for the proportion of English-language published reports for the 9 SR-included reports (the present study although SR-included is excluded from this comparison) in Table 5.4; or the excluded (Table 5.3);

$X^2 = 3.52$: 1df; $P > 0.05$. The clinical and radiological features extracted from each of the series are distributed in Tables 5.4 and 5.5 respectively. A synthesis of the 9 SR-included series is compared statistically to the present study in Table 5.7.

A total of 10 reports survived the selection criteria and were accepted for the SR (Table 5.4). There were no Latin-American reports. Of the 482 cases there were 198, 107 and 117 in Black, Caucasian and Oriental (mainly Japanese) patients respectively. Eighty percent of Black patients were Americans; details within the 3 mixed Caucasian and Black groups were inadequate to permit comparison between their genders, presenting complaint or site affected.

Although 5 of the 10 reports were Oriental, their sample sizes were smaller; the 5 Oriental reports ranging between 14 and 29 cases had a mean of 23.40 (sd 16.99), in contrast to 2 Western reports with a mean of 125.50 (sd 171.83); the difference was not significant ($t = 0.84$; 1df; $P > 0.05$). The 'number of FocCODs per hospital per year' varied widely from 0.6 for the Hong Kong Chinese to 20.0 Su and co-authors' (1997a and b) American report. The 3 Japanese reports varied from Matsuzaka and co-author's 0.7 through Miyamoto's (1996) 2.2 to Ohkura's (2001) 3.6. The reports on the Hong Kong Chinese and Matsuzaka and co-authors' (2002) Japanese had similar 'number of FocCODs per hospital per year'.

In Table 5.4, the percentage of reports with details available varied greatly from 90% (9 reports) for gender to 30% (3 reports) each for the presence of pain (or

Table 5.4. Focal Cemento-Osseous Dysplasia: Systematic review; Analysis of the included reports.

First Author (year)	National and/or Ethnic origin (Number of Hospitals(H) and number of Cities(C))	Period covered	No. of Focal CODs (No. per hospital per yr)	Gender		Age mean (range) in years	Presenting Signs & Symptoms			SITE		Comments
				Males	Females	Pre-Presenting duration mean(range) in years	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Terms used for FocCOD in text
Eversole (1972)	US (1H1C)	ING	19	2*	17(5*)	ING teeth (>9>50) edent (>19>50)	ING	ING	ING	17(7*)	2	Part of a FOL series. *5 with teeth
						ING						PCD (with teeth) cement.
Sakota (1977)	Japanese (1H:1C)	ING	14*	1	13	**44**(18-66) 1M 18 yr F46.3(28-66)	8	6	1 incidental	1 11	2 2	*16 cases Part of a FOL series.
						ING						PCD
Slootweg (1990)	Dutch (1H:1C)	ING	4	0	4	**40**(ING)	ING	ING	ING	4	0	Part of a FOL series.
						ING						Loc PLD-FOL
Ackermann (1992)	South Africa (1H:1region) (B64%; W36%)	ING	63	4	59	ING	ING	ING	ING	IIG	IIG	3 Paget's cases 3 TBCs
						ING						Gigantiform cementoma

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Gender Males Females	Age	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Comments
Summerlin (1994)	US (1H:1C) (B32%*; W58%)	ING	120*	IIG*	IIG*(ING)	0	0	120 incidental	IIG	IIG	*for 221 cases Only 120 cases had radiographs
					ING						FocCOD
Miyamoto (1996)	Japanese (1H:1C)	1976-1995 10 years	22 (2.2)	3 19	**41** F:41.8 (21-60) M:34.7 (28-46)	ING	ING	ING	0 21	0 0	3 other catagories were not included
					ING						FocCOD
Su (1997)	US (1H:1C) (B64%;W32 %)	1982-1994 12 years	247 (20.0)	33 214	**38**(10-79)	90 Some swelling with mild discomfort		152 incidental	57 152	10 24	Part of a FOL series.No jaws for 3 cases
					ING						FocCOD
Ohkura (2001)	Japanese (1H:1C)	1976-2000 14 years	51*(3.6)	7 44	**52**(27-84)	13	22	7 incidental	0 (50*)28	4*	* 4 affect both jaws
					ING						LocalCOD
Matsuzaka (2002)	Japanese (1H:1C)	1966-2001 35 years	24 (0.7)	5 17	IIG	ING	ING	ING	0 13	1 10	
					ING						PCD
Present study	Hong Kong	1982-1992 10 years	6 (0.6)	0 6	**52**(37-65)	0	3	2 incidental 1 numb	0 6	0 0	
					ING						cementomas
Total number of cases			570	55 [b] 393 [b]		111 [d]	121 [e]	284 Incident. [f]	332 [g] 58 [h] 231 [h]	55 [g] 13 [h] 36 [h]	
Percent of cases				12 88	**41** [c] (10-79)	25	28	65	86	14	

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Gender Males Females	Age	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Comments
Total number of series			(5)[a]	8	7 (4) *0(0)*	5	5	5	7		
Percent of 10 series			(50)	80	70 (40) *0(0)*	50	50	50	70		

Abbreviations and Notes: ant, anterior; B, Black; C, City; CF, Cementifying fibroma; cement.;cementoma; FocCOD, focal cemento-osseous dysplasia; FU, Follow-up; H, Hospital; LocalCOD, Localised cemento-osseous dysplasia; Loc PLD-FOL, localised periodontal ligament-derived fibro-osseous lesion; O, oriental/ East Asian; OF, ossifying fibroma: IIG, inadequate information given; ING, Information not given; Incid, incidental finding; PCD, periapical cemental dysplasia; post. posterior; recur, recurrences; TBC, traumatic or simple bone cyst; W, White/Caucasian; yr, year/s

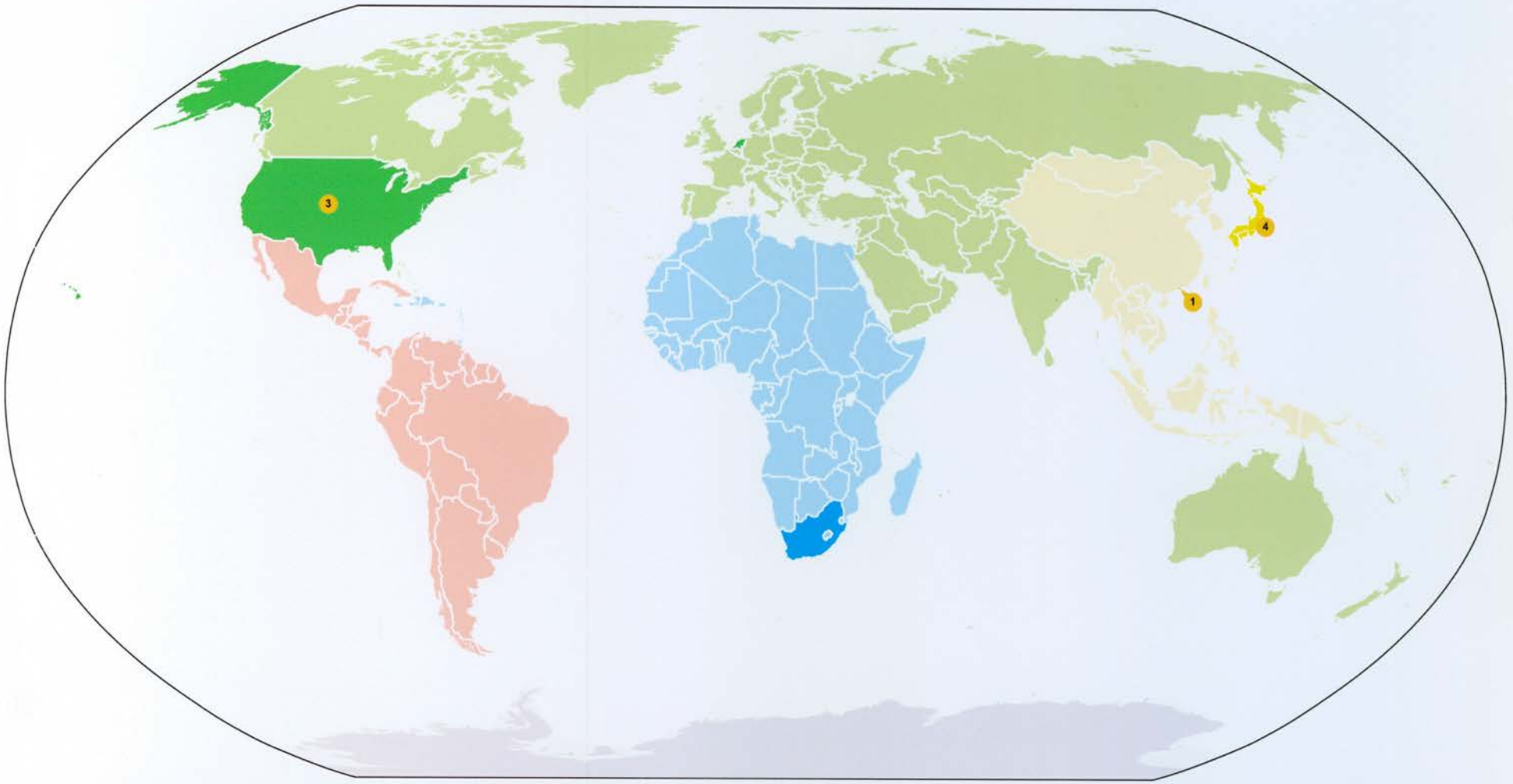
Key	Number of reports	Total number of cases
a. No.COF/H/yr	5	350
b. Gender	8	448
c. Mean Age	6	344
d. Swelling	5	439
e. Pain	5	439
f. Incidental	5	439
g. Site: Jaw	7	387
h. Site:Ant./Post	6	Md:289; Mx: 49
i. Follow-up/ Recurrence	0	0

Table 5.5. Focal Cemento-Osseous dysplasia: Systematic review; Analysis of the radiology of the included reports.

Author (year)	No.of cases	Predominant Radiographic Presentation			Patterns of the Radiographic Margins			Association with Teeth(Yes!)or Edentulous Areas (No!)		Root Resorption And Tooth Displacement	
		Radio-lucency	Radiopacity within Radiolucency	Opaque	Well-Defined Without Sclerosis	Well-Defined With Sclerosis	Poorly-Defined	Yes	No	Yes	No
Eversole (1972)	19	2	17	0	*19*[b]		*0*[b]	7	12	ING	ING
Summerlin (1994)	119	52	47	20	*Contradiction*			IIG	IIG	ING	ING
Su (1997)	142	44	34	64	45	30	67	IIG	IIG	0	142[a]
Ohkura (2001)	51	5	23	23	ING	ING	ING	27	24	ING	ING
Present Study	6	2	3	1	6	0	0	1	5	0	6
Summary	337	105	124	108	51	30	67	35	41	0	148
Percent		31%	37%	32%	35%	20%	45%	46%	54%	0	100%
		Percentage of 337 cases			**Percentage of 148 cases**			**Percentage of 76**		**Percentage of 148**	

Abbreviations and Notes: [a], by inference from context; [b] ,excluded from calculations; IIG, Inadequate information given; IIG; ING, Information not given.

Statistical Analysis: Chi-square	
Predominant radiological presentation: Eversole and Summerlin	X^2 = 16.68: 2df: P < 0.001
Predominant radiological presentation: Eversole and Ohkura	X^2 = 9.08: 2df: 0.05 > P > 0.01
Predominant radiological presentation: Eversole and Su	X^2 = 33.90: 2df: P < 0.001
Predominant radiological presentation: Summerlin and Su	X^2 = 23.97: 2df: P < 0.001
Predominant radiological presentation: Summerlin and Ohkura	X^2 = 23.80: 2df: P < 0.001
Predominant radiological presentation: Su and Ohkura	X^2 = 158.88: 2df: P < 0.001
Association with teeth: Eversole and Summerlin	X^2 = 1.40: 1df: P > 0.05



Map 2. Focal Cemento-osseous Dysplasia: Global distribution of 10 Systematic Review-included series of cases coloured according to group

Map 2.

mild discomfort) or swelling in the 570 cases of FCOD. Five, 4 and 1 reports were of Oriental, Western and African communities respectively. Their global distribution is displayed on Map.5.1. Eighty-eight percent of the 448 cases that identified gender was female; there were no differences between males and females for with Oriental and American reports and between the present study and the rest of the SR. (X^2 = 0.07 and 0.8 respectively; 1df; $P > 0.05$).

The mean age for the present study was 53.5 (sd 9.4) whereas that for the 344 cases in the SR was 41 years. A mean age of 47.2 years was observed in three of four Oriental series, in comparison to 39.0 years for the Western (Su et al., 1997a and b; Slootweg and Muller, 1990): $t = 2.77$: 2df: $P > 0.05$.

Seventy-one percent of 487 cases were discovered incidentally to the investigation of a separate complaint. Significantly fewer cases in the present study were found incidentally than the rest of the SR. Pain and swelling 25% and 28% respectively; occurring together most of the time because the largest report (Su et al., 1997a and b) stated that 38% displayed "some swelling with mild discomfort." The present study displayed no difference with regards to swellings and pain compared with the rest of the SR.

In Table 5.5, although the 3 predominant radiographic patterns are almost evenly distributed in the overall synthesis, this is clearly not so as each of the 4 larger reports varies significantly with any other in this regard. There is no significant

difference between Summerlin and Tomich's[4] and Ohkura's[33] reports with regards to whether the lesions are associated with dental or edentulous areas.

The present study's predilection for presenting with a well-defined margin was its only feature to differ significantly from that of the rest of the SR (Table 5.6.). There was a significant difference between Orientals and Americans with regards to the predilection of Americans for the posterior mandibular sextants. (X^2 = 24:9; 3df; P < 0.001).

Table 5.6: Focal Cemento-Osseous Dysplasia: Chi-square statistics

Feature	Hong Kong	Rest of SR	X^2	Dg. fre	P
Gender:Male:Female	0:6	55:387	0.80	1	> 0.05
Jaw: Mandible:Maxilla	6:0	326:55	0.26	1	> 0.05
Swelling:Yes:No	0:6	111:322	2.06	1	> 0.05
Pain: Yes:No	3:3	118:115	0.00	1	> 0.05
Incident.Find:Yes:No	2:4	282:151	2.67	1	> 0.05
Predom.Radio.Present.	2:3:1	103:121:107	0.72	3	> 0.05
Well-defined:Yes:No	6:0	67:75	6.25	1	0.05>P>0.01
Assoc w Teeth:Yes:No	1:5	34:36	2.19	1	> 0.05
RootResor/Displ:Yes:No	0:6	0:136	0.00	1	> 0.05

Abbreviations: Assoc w teeth, associated with teeth; Incident.Find, incidental finding; Dg.Fre, degrees of freedom; Predom.Radio.present, predominant radiological presentation; RootResor/Displ, root resorption /displacement; SR, systematic review.

DISCUSSION

Five reports did not cite Summerlin and Tomich's (1994) report, but were included on the alternative grounds already addressed in the introduction. The

principal overriding aim of this study was to include as many reports and/or as much of each report as would be consistent with the inclusion criteria of being histopathologically confirmed as FOLs, did not contradict the surgical specimen criteria, radiologically confirmed as FocCODs, and representing a series of cases derived from a community. Every SR carries within it the seed of its successor, which upon reflection and further reports should provide clearer and more refined answers. This will be discussed latter.

The degree of margin definition was not made an issue for this SR. While all FocCODs in the present report were well-defined, this was not observed in other reports. Summerlin and Tomich (1994) stated in the text that lesions were 'ill-defined', but in their summary they were "fairly well-defined", whereas Su and co-authors (1997b) reported that nearly half were poorly-defined. As no objective method was used, it could be that Su and co-authors' (1997a and b) FocCODs have been deemed to poorer-defined in relation to their COFs (COF by their essential WHO definition must be well-defined (Slootweg and El Mofty, 2005)), also considered in the same report. Review of Ohkura's (2001) descriptions and figures would suggest that almost all of his FocCODs were well-defined. Use of an objective parameter, such as that by Slootweg and Muller (1990) in future reports will clarify this matter.

The radiological contribution was confined to ensuring that the FocCOD were really focal or localized and not part of an otherwise undiagnosed FCOD. Most of the SR-included reports did not expressly state that FCOD had been excluded, this

was presumed to have happened by their reference to Summerlin and Tomich (1994) or declaration that that the lesions were solitary or localized or focal. Clearly the word 'localized' is open to a wider interpretation; it can be localized to one side of the face as well as to a region of a jaw. The former may have been Ohkura's (2001) interpretation.

Although the significant difference in 'numbers of FocCODs per hospital per year' between the Japanese and American reports may in part be explained by Reichart and co-authors' (2005) observation that their reports are based on the treatment of different groups of patients within their communities (This will be discussed more fully later.) These two nations, both world leading democratic states, differ markedly in ethnicity, culture and by health care systems; Japan's are more homogenized whereas America's are more diverse. This is reflected in Su and co-authors' (1997a and b) American report in which two-thirds of their patients are Black whereas only a third of Summerlin and Tomich's (1994) are Black. Once the 7% of all specimens derived from Black patients in Summerlin and Tomich's (1994) report is weighted by their representation in the community (upon which the report was based), for the 141 White cases there could be as many as 500 Black patients affected with this lesion.

Although series of FocCOD in Oriental communities appear just as frequently reported as those with substantial Black communities, the former's very low 'number of FCOD cases per hospital per year' values in comparison with those

of the latter's would indicate that the frequency of FocCOD in Orientals may be lower than that experienced in reports incorporating substantial Black communities.

Reiterating the FCOD discussion concerning the significant association between edentulous areas and COD lesions, which could contribute a secondary infection and therefore symptoms, Waldron and co-authors (1975) claimed that most of their symptomatic cases had been "edentulous in the affected areas for many years"; all their 10 biopsies from edentulous sites had symptoms, whereas the four from dentate areas had none. Therefore, a significantly higher prevalence of pain in Oriental reports (Sakota, 1977; Ohkura, 2001) may reflect this association between lesions in edentulous areas; otherwise the essential character of FocCOD is to remain symptom-free unless secondarily infected.

Waldron and co-authors (1975) considered this later onset to occur secondary to the exposure of the cemental masses following resorption of the edentulous alveolus, or by extraction of teeth with roots close to the lesions. The observation of these lesions at sites of extraction, therefore, may in part explain their presentation. Infection of these lesions may provoke a chronic sclerosing osteomyelitis; Waldron and co-authors (1975) reported that true chronic osteomyelitis could appear similar to COD radiographically.

Su and co-authors (1997a and b) reporting the largest FocCOD study pronounced it as the most common FOL in the oral and maxillofacial area region. Nevertheless, despite their 20 'FocCODs per hospital per year' it represented only

0.4 % of their all-surgical specimen. Nevertheless, it is very unlikely that a FocCOD lesion that is symptomless and otherwise diagnosed on clinical and radiological evidence will be operated upon today and the resultant specimen referred for a histopathological evaluation. Until Summerlin and Tomich (1994) substantially characterised this lesion it would have been largely unrecognized. This is reflected in the differential diagnoses of the present report and that by Sakota (1977b). Sakota (1977b) reported that of his 14 cases, 5 were considered as osteomas, 4 as odontogenic tumours, 2 as osteomyelitis, and 1 a cyst and 2 as other unspecified diagnoses. In the present report, although only of 6 cases, it is difficult to understand why 2 were considered to be cementoblastomas as not one displayed root resorption. As the FocCOD becomes more widely recognized fewer will be removed, and the large numbers present in the histopathology files of Summerlin and Tomich (1994), and Su and co-authors (1997a and b) are likely to become a historical phenomenon, unless their elective removal may be required to prepare the site for osseointegrated implants.

Following recalculation of Ohkura's (2001) data, FocCODs were discovered more frequently when not related to teeth ($X^2 = 6.07$; 1df: $0.05 > P > 0.01$). The present study confirms the observation by Waldron (1985) that FocCOD is localized in particular to edentulous areas of the posterior mandible, and that thus may be also be seen to a lesser degree for the generalized lesions. Therefore, since many occur at sites of previous extraction, they may partly represent, as suggested by Waldron (1985), the end-stage of an abnormal reaction of bone to injury.

Ohkura (2001) reported that the degree of calcification observed radiographically was not related to the mean age, but to the grade of histopathological maturation. Nevertheless, according to his Figure 7, radiolucencies occurred in younger patients and complete radiopacities in older patients.

Summerlin and Tomich (1994) recommend follow-up of these lesions, because 2 of their lesions progressed to FCODs. A tendency for a patient already with at least one COD to acquire more has also been revealed by Kawai and co-authors (1999). Although it is clear the surgeons in Ohkura's (2001) report are following up his cases radiographically no comment was made about the outcomes of this follow up.

An aim will be that one day the FocCOD will be recognized a clinical entity that does not require treatment and certainly not biopsy. In the meanwhile this lesion should be better characterised. The reports by Summerlin and Tomich (1994) and Su and co-authors (1997a and b) have substantially achieved this retrospectively. Prospective follow-up is required, along the lines set up by Kawai and co-authors (1999). The clinician will want to be sure that these lesions, although perceived innocuous at that moment, do not incur problems latter. Although there has been follow-up of these lesions it has not been for long periods. Furthermore, the ageing population increases the need for prosthodontic treatment, increasingly accompanied by implants. Implants, in turn, require at least reasonable bone quality for success. Clearly an area occupied by a FocCOD could not be realistically considered for implant placement. Therefore, consideration must be given to the possibility that

these lesions may need to be removed in order to prepare that site to receive an implant. At this point, we have very little information about post-surgical healing of sites formerly occupied by CODs. We do not know if they recur. Even if they do heal, we do not know if the bone in the healed area will be of optimal quality for implant placement. MacDonald-Jankowski's report (1995) on traumatic (simple) bone cysts (TBCs) within the same Hong Kong Chinese community served by PPDH revealed that 2 cases recurred; one displayed multiple recurrences eventually running throughout the entire body of the mandible. This reference to TBCs in the context of a study on FocCODs is very relevant, because their association is well established (Horner and Forman, 1988).

Another point raised, particularly by Kawai and co-authors (1999), is the presentation of some of these lesions as complete radiopacities. This is precisely the appearance of idiopathic osteosclerosis (IOS). MacDonald-Jankowski's SR (1999) revealed that these were more prevalent in the Hong Kong Chinese than in two British communities. They were by definition symptom-free. In addition there may be an association between the IOS and fluoridation of the water supply (Evans et al., 1987). A higher incidence of dental fluorosis was observed in the Chinese than in Caucasians of European or Indian descent (King and Wei, 1986). A similar high incidence of dental fluorosis was observed in the Japanese (Yonetsu et al., 1997). The staple diet of both Chinese and Japanese is generally high in fluoride (King and Wei, 1986; Monoguchi, 1970). As to whether fluoride contributes to CODs in these Oriental communities has not been answered yet. Nevertheless, analysis of any CODs or IOSs removed for histopathology should include titration for fluoride.

FocCODs fall into the differential diagnosis of COFs, which have already been the subject of a comparative study by Summerlin and Tomich (1994). They found FocCOD more prevalent than COF. This finding would also be supported by Su and co-authors (1997a and b), regardless of whether their 15% of compromised cases of COF were to be identified and removed. In Hong Kong only 6 FocCODs were found in contrast to 19 COFs referred for histopathology. Two out of these 6 were found as incidental findings. This and the fact that the overwhelming number of FocCODs in the SR were incidental findings, would suggest that they infrequently are associated with pain and swelling which may led to their discovery. While it is likely that many were observed during the initial examination including panoramic radiography in 80% of patients attending PPDH between 1981 and 1990, the vast majority, which would have been symptomless, would have not been considered as treatment priorities at that time.

Furthermore, failure to identify these lesions as FocCOD could also result to their presence in histopathological files. It is clear from the provisional and differential diagnoses of the 6 Hong Kong lesions that the surgeons considered that they were confronted by lesions that required surgical removal. The term 'cementoma' at the time was not only widely synonymous with COF but even 'cementoblastoma'. Therefore misdiagnoses may have contributed to many of symptomless lesions derived from histopathological files reported by Summerlin and Tomich (1994) Su and co-authors (1997 a and b).

The presence of a radiolucent-stage COD at the apex of a tooth looks similar to a periapical radiolucency caused by pulpal necrosis. Such cases have on occasion required surgery to determine their nature (Wilcox et al., 1981; Drasic et al., 1990). On occasion they have been associated with simple bone cysts (Horner and Forman, 1988; Mupparapu et al., 2005).

Miyamoto (1996) classified CODs into 4 categories on the basis of variant histopathological presentations. Unfortunately, because their radiological features or details of their follow-up were not included in the report very little can be inferred about their behaviour. Similarly Su and co-authors (1997a and b) reported FocCODs displaying well and poorly-defined margins, but there was little to determine whether this difference was associated with any particular outcome. There was no mention of follow-up. Although it is likely that some of Su and co-authors' FocCODs would progress to FCODs, as suggested by Kawai and co-authors' (1999) report, such short-term follow-up is inadequate for the growing activity in implantology. The presence of CODs appears to contraindicate osseointegrated implants. Therefore, a better understanding of the natural history of these lesions is required. This can be derived from long term follow-up both of those lesions, which have been surgically treated, and those, which have not. For those treated, it would be invaluable to know when normal healing follows, and whether the quality of the healed bone is adequate for implants.

CONCLUSIONS

1. The response to the PICO question remains unclear, because there are inadequately detailed reports, particularly with regards to radiology and follow-up

2. The two at-risk global communities appear to be Blacks and Orientals.

3. The Hong Kong Chinese are significantly more likely to present radiologically with well-defined margins.

4. As with FCOD the maturation progress of FocCOD has not been established; a longitudinal review of FocCOD cases could determine their progress and sequelae, particularly with regard to edentulous areas. A better understanding of these could enhance dental management of increasingly ageing populations, particularly in the West (where the majority of reports regarding Blacks originate) and in the Orient. This better understanding is necessary because FocCOD has a more extensive differential diagnosis. The diagnostic problem among FOLs would now exist between FocCOD and COF rather than between COF and FD. The fact that FocCODs are observed more frequently in the at-risk communities enhances their clinical importance.

Chapter 6.

CEMENTO-OSSIFYING FIBROMA

INTRODUCTION

The previous synthesis confined to English language papers on COFs included only 11 reports amounting to 535 individual cases (MacDonald-Jankowski, 1998). The first edition of the WHO classification (Pindborg et al., 1971) was clear that FD and COF can be distinguished by radiology; the former has a poorly-defined margin, whereas the latter has a well-defined margin. The Slootweg and Muller's (1990) radiological test described earlier had not been applied in this synthesis, which was not a SR. The present SR was considerably more extensive including reports in major world languages and some lesser-used European languages. It reported also the clinical and radiological manifestations of 24 cases of COFs affecting the jaws of a largely Chinese population and compared these with the 650 cases found in 26 published SR-included reports.

The classical three stages in the radiographic appearance of the COF, like other fibro-osseous lesions, generally reflect the underlying histopathology, which in turn depends on the maturity. The initial appearance is radiolucent, which then becomes progressively more radiopaque as the stroma mineralises. Eventually, the individual radiopacities coalesce to the extent that the very mature lesion may appear sclerotic.

AIMS AND RESEARCH QUESTIONS

The primary research question for this SR, or PICO question, is "Do other clinical and radiological features improve diagnosis of COF compared with well-defined margins?"

Initially this question was framed so as to distinguish further COF from FD. In order to answer this question only those reports, which consider a well-defined margin of a histopathologically confirmed FOL as a COF, can be admitted to this SR. In addition to this question there are other supplemental questions, which help to frame the selection criteria for the above PICO question; these are: -

Question 1: "What are the clinical and radiological characteristics observed in a largely Southern Chinese Hong Kong community?"

This requires a detailed analysis of the clinical and radiological features observed in a continuous series of cases of COF lesions in a Hong Kong Chinese community admitted to PPDH.

Question 2: Do the Hong Kong Chinese have a different presentation of COF compared with the rest of the SR?

Comparison of the Hong Kong Chinese with the rest of the SR will be addressed in this chapter. Comparison of the Oriental communities with regards to other global communities will be addressed in Chapter 8. To assist the formulation of an answer the SR-included reports will be divided into four global groups, Western, African, Oriental and Latin-American, broadly reflecting ethnic origin.

MATERIALS AND METHODS

A: Histopathological-file-based Hong Kong study

The histopathological files of PPDH between 1982 and 1992 revealed 20 cases of COF affecting the jaws for which the clinical notes and radiographs were available; a further 4 from 1992 to 2004 were added. The clinical notes and radiographs of each case were retrospectively reviewed. In order to diminish the effects of 'expectation bias', which is intrinsic to a retrospective review of cases, the radiographs were read prior to the clinical notes. Each patient's ethnic origin, sex, age, clinical history and findings on examination and the differential or provisional diagnosis were obtained from the clinical records. The definitive diagnosis of a COF was made on the basis of both the histopathology and the radiology. Each COF was radiographed in two planes. Panoramic and periapical radiograph were available for all cases. Every mandibular case was accompanied by a true occlusal and oblique anterior radiographs were available for all lesions in the anterior region in both jaws. Occipitomental and lateral sinus views had been obtained for the two cases involving the maxillary antrum. The radiographs were viewed on a standard illuminated screen, sited in reduced ambient lighting, and assessed by a single investigator. The influence of the COF on adjacent structures, such as the teeth, the buccal and lingual cortices, lower border of the mandible and the maxillary antrum, was noted. The outline of the COF was defined as the well-defined boundary between the normal adjacent bone and the lesion, according to the objective test established by Slootweg and Muller. The outline of the COFs was then traced by the cursor of an image

analyser (Kontron Bildanalyzer, Carl Zeiss Far East Co. Ltd., Hong Kong) and the area expressed in cm^2.

The measurements were made directly from either the intra-oral or panoramic radiographs. Although periapical radiographs were available in every case, they were not generally used for measurement because of their frequent inability to encompass fully the whole lesion. Therefore most of the measurements were made from the panoramic and standard anterior occlusal radiographs; the latter were exclusively used for lesions anterior to the canines. The values obtained from the panoramic radiographs were corrected for the measured values derived from it; they were adjusted for a magnification factor of 1:1.2 (Panelipse, GE, Milwaukee, USA). Observer self-calibration was achieved by comparing values derived for 20 measurements produced on two separate occasions in 1992; the reproducibility was in excess of 95%.

The histopathological reports were reviewed for the precise terminology, whether it was, cementifying fibroma (CF), ossifying fibroma (OF) or cemento-ossifying fibroma (COF) to gain an insight to the relative proportions of osteoid and cementoid structures. The original histopathological material was not reviewed.

B: Systematic review

A SR is required to answer the PICO question. A SR requires not only a literature to search, but also selection criteria to sift this literature. As the primary

aim is to include as many reports as possible a wide search of the literature will be made, including non-English reports.

Selection Criteria

There were 3 inclusion (Criteria 1 to 3) and 3 exclusion (Criteria A to C) criteria for the SR. Each report will pass through these criteria in strict sequence. Although a report may be excluded by more than one criterion, only the first criterion to exclude a particular report will appear in Table 6.5. [For the sake of brevity only those reports which cannot be readily included from their title or abstract will be discussed and cited.]

'Exclusion' refers to the 'non-inclusion' of a report within the SR and will be used regardless of whether it is in relation to either 'inclusion' or 'exclusion' selection criteria.

Inclusion Criteria:

Criterion 1. Consistency with the WHO classification.

The lesions had to be consistent with the histopathology at least that established by the first edition of the WHO's classification of odontogenic tumours for CF (or its synonyms) and OF (Pindborg et al., 1971). Although Waldron and Giansanti (1973b) soon after developed this further to consider CF and OFs as part of

a COF spectrum, which the WHO's second edition (Kramer et al., 1992) reaffirmed. In absence of a description of the histopathology, reference to any of the above authorities would be adequate for this purpose. Nevertheless, this is a rebuttable presumption. It is a minimal expectation that for inclusion a report should at least report both CF and OF forms.

Criterion 2. The definition of the margin on radiographs.

Although this is essentially part of 'Criterion 1', because the histopathology and radiological appearances were addressed equally, it is essential that radiological description at least of the periphery be included in the reports to be included in the SR. It is assumed that the radiographs would be available to the reporters. If the radiographs were not available then radiological description of good marginal definition in clinical notes would be adequate for inclusion. Although it is appreciated that reporters may have used different parameters by which they had determined marginal definition, and they may not have used an objective parameter such as that developed by Slootweg and Muller (1990), reasonable allowance is made to admit reports that may have reported some COF margins as poorly-defined. If the report was reported in sufficient detail then it may be possible to identify the non-conforming cases and delete them, thus allowing the rest of the study to pass this criterion. If this were not possible, such studies could only pass this criterion if they do not exceed 10% of the lesions reported as poorly-defined. Studies which reported that 'almost all' or 'the overwhelming majority', of the cases were 'well-defined' would be construed as meaning between 90% to just below 100% (that is within the

already described 10%) and be admitted. On the other hand studies reporting that 'most' or 'majority' of the cases were well-defined would not be admitted, because these and similar phrases would be construed to represent 51% to 89% and be thus well outside the 10% allowance.

Criterion 3. A complete collection of cases of COF.

The study should represent a complete collection of cases of COF, arising within a particular community, occurring in the reporters' caseload. Reports that were merely a selection of cases such as case reports and those studies, which were primarily concerned with specific investigations or a discrete age group, such as children or a particular jaw, were excluded.

Criterion A. Excludes reports already reported and included in the SR.

It prevents doubling reporting of the same clinical cases, by excluding those reports whose data has already been reported and included in the review. It also excludes reports covering the same clinical material, unless the degree of overlap does not exceed 50%, and that there is at least one statistically different feature between them.

Criterion B. Excludes extragnathic cases

In order to include only data that pertains to the jaws, it excludes those reports with extragnathic cases:

a. Their details could not be identified and deleted, and,

b. They exceed 10% of the cases.

c. If the 10 % allowance is exceeded then the whole report will be excluded unless there remains at least one feature that clearly refers only to the jaw lesions. Then the report will be included only with regard to that feature.

Criterion C. Excludes referred cases

It reinforces 'Criterion 3' by minimising dilution of the data arising primarily within a specific community, it excludes those reports which include referred cases, displaying unusual features that may skew the profile of COF within that community, which would in turn skew the SR, if: -

a. Their details could not be identified and excluded, and,

b. They exceed 10% of the cases.

The electronic database interrogation

The PubMed interface of Medline and LILACS were interrogated by the following keywords, "Cemento-ossifying Fibroma", "Ossifying Fibroma" and "Cementifying Fibroma". This was supplemented by a hand-search of journals listed

in Table 3.1. This strategy was further augmented by reference to the bibliographies (or citation lists) of all reports identified by Medline or hand-searching.

Definition of parameters.

The number of years is calculated on the assumption the study begins on the January of the beginning year and ends on the December of the closing year unless stated otherwise in the text.

The 'number of COFs per hospital per year' reflected the number of hospitals contributing to the report and the number of years from which the reported series was derived. Unless it is otherwise clear in the report, the study period at each hospital in a multi-centre report will be assumed to be the same. The advantage of assessing the 'number of COFs per hospital per year' is the ease of comparison of the number of lesions diagnosed as COFs in each hospital (or the average hospital in a multi-centre report) in the course of the average year.

The jaws were further divided into posterior (molar and premolar) and anterior (incisors and canines) sextants. Although the demarcation point between these areas was infrequently expressed, it was taken to occur at a vertical line just distal to the distal surface of the canine.

The lower border of the mandibular alveolus is set by the inferior dental (mandibular) canal and the upper border of the maxillary alveolus on panoramic radiographs is set by the image of the hard palate on panoramic radiographs or lateral cephalographs (MacDonald-Jankowski, 2004a).

Significant differences in frequencies were tested by the X^2 test with $P < 0.05$. Significant differences in age and size were tested by a Student's t-test with $P < 0.05$.

RESULTS

A: Histopathological file of COF cases affecting the Hong Kong Chinese.

All cases were female. The details of the histopathological presentation, age, clinical presentation or complaint, size and distribution of the 24 COFs in the present study are shown in Table 6.1. Their radiological features, provisional and differential diagnoses, details of their follow-up and recurrence are set out in Tables 6.2, 6.3, and 6.4 respectively.

The age at presentation is wide (10-80 years, mean 37.71, sd 14.74 years). The mean ages for the mandible and maxilla are 39.35 (sd 15.07) years and 29.50 (sd 10.88) years, respectively ($t = 1.54$; 22df; $P > 0.05$). Most were found in the third and fourth decades in Table 6.7. The decade distribution of their histological presentation

is in Table 6.8. This mean age at first presentation at PPDH was higher than that of the SR (Table 6.6), and remained even so when prior awareness of the lesion (Table 6.1) is taken into account, reducing the mean age to 35.90 years (sd 15.77; n = 19), following exclusion of the non-contributory Mandibular Cases 4,6,8,18 and19). Fourteen of these 19 cases were observed as incidental findings on panoramic radiographs prescribed for the assessment of other dental reasons, which would have provoked their attendance at PPDH (Table 6.1).

The two main modes of presentation (Table 6.1), incidental finding and swelling presented at 38.88 (sd 12.54) and 32.5 (sd 10.52) years respectively. Only one of the four referred patients had been specifically referred by her general dental practitioner for investigation of the symptoms and signs associated with the COF (Mandibular Case15). The 3 cases associated with pain occurred significantly in the oldest patients (50.3 sd 5.7 years) in comparison with the 21 non-pain cases (36.36 sd 14.80; $t = 3.13$; 22 df; $0.01 > P > 0.001$).

Twelve lesions occurred in the posterior mandible, 6 in the anterior mandible, 1 crossed from the anterior sextants into the posterior sextants bilaterally, and another unilaterally, 3 in the posterior maxilla and 1 in the anterior maxilla (Table 6.1).

TABLE 6.1. Cemento-Ossifying Fibroma: Hong Kong Patients; Gender, age, presenting complaint, size and site.

Case No. & *Histopath.*	Gender & Age(years)	Presenting Complaint	PriorAwareness (years)	Size (cm^2)	Right 8 7 6 5 4 3 2 1	Left 1 2 3 4 5 6 7 8
Maxilla						
1. *OF*	F 18	swelling	0.5	N-M	I----------I	
2. *OF*	F 26	Incidental	0	N-M		I----------I
3. *OF*	F 30	Incidental	0	1.18	I----I	
4. *CF*	F 44	Incidental	0	4.09		I----------I
Mandible						
1. *COF*	F 10	Incidental	0	4.23	I----------I	
2. *CF*	F 21	Incidental	0	4.15		I-------I
3. *COF*	F 26	Swelling	1	5.76	I----------I	
4. *COF*	F 26	Loose teeth	ING	10.15	I----------I	
5. *CF*	F 28	Incidental	0	1.44	I---I	
6. *COF*	F 29	swelling	Gradual swelling	11.12		I----------I
7. *COF*	F 33	Incidental	0	1.39	I-----I	
8. *COF*	F 35	swelling	ING	3.01	I-----I	
9. *CF*	F 37	Incidental	0	2.48	I----I	
10. *CF*	F 38	Incidental	0	1.77	I-----I	
11. *COF*	F 39	swelling	2	1.42	I-----I	
12. *OF*	F 39	Incidental	0	1.54		I-----I
13. *OF*	F 44	Pain,Swell	0.4	12.32	I----------I	
14. *CF*	F 45	Incidental	0	2.25	I----------I	
15. *CF*	F 48	Swelling	10	1.75		I---I
16. *CF*	F 50	Incidental	0	7.70		I----------I

Case No. & *Histopath.*	Gender & Age(years)	Presenting Complaint	PriorAwareness (years)	Size (cm^2)	Right 8 7 6 5 4 3 2 1	Left 1 2 3 4 5 6 7 8
17. *COF*	F 52	Incidental	0	8.24	I----------I	
18. *COF*	F 52	Pain	ING	4.90	I---------- -----I	
19. *CF*	F 55	Pain,Swell,U	ING	1.59	I----I	
20. OF	F 80	Incidental	0	3.80	I----------I	

Abbreviations and Notes: CF, cementifying fibroma; COF, cemento-ossifying fibroma; enlarg. Enlargement; Histopath., histopathology; Incidental, incidental finding; ING, information not given; No., number; OF, ossifying fibroma; swell.swelling; U. ulcer.

Table 6.2. Cemento-Ossifying Fibroma: Hong Kong Patients; The radiological features.

Case No. / Gender & Age	Predominant radiodensity			Other Radiological features								
	Radio-lucent	Central Opacity	Number of Opacities	Shape	Margin Definition	Cortex Present (+sclerosis (S))	Expansion	Specific Anatomical Features		Inferior dental canal(IDC) Displaced?	Tooth Resorption	Tooth Displacement
Maxilla								Reduction of Maxillary Antral Lumen				
1. F 18	No	Yes-**fillsMA**		N/A	Well	Yes	Yes	Yes		N/A	IIG	Yes
2. F 26	No	Yes-**fillsMA**		N/A	Well	No	Yes	Yes		N/A	No	No
3. F 30	No	Yes	1	Od	Well	No	Yes	No		N/A	No	No
4. F 44	No	Yes	1	Od	Well	Yes	Yes	Yes		N/A	No	No
Mandible								Inferior border of the mandible Displaced	Thinned			
1. F 10	No	Yes	1	Rd	Well	No +S	Yes	No	No	Yes	No	Yes
2. F 21	No	Yes	1	Rd	Well	Yes	Yes	Yes	Yes	Yes	No	No
3. F 26	No	Yes	1+	Rd	Well	Yes	Yes	No	Yes	N/A	No	Yes
4. F 26	Yes	No	0	Mult	Well	Yes	Yes	Yes	No	N/A	No	Yes
5. F 28	No	Yes	1	Rd	Well	Yes	No	No	No	N/A	No	No
6. F 29	Yes	Yes	0	Od	Well	No +S	Yes	Yes	No	Yes	No	Yes
7. F 33	No	Yes	1	Rd	Well	No	No	No	No	No	No	No
8. F 35	Yes	No	0	Rd	Well	Yes	Yes	No	No	No	No	No
9. F 37	No	Yes	1	Rd	Well	Yes	No	Yes	Yes	Yes	No	No
10. F 38	No	Yes	1	Mult	Well	No +S	No	No	Yes	Yes	No	No
11. F 39	Yes	No	0	Rd	Well	Yes	Yes	No	No	No	Edent	Edent
12. F 39	No	Yes	3	Rd	Well	Yes+S	No	Yes	No	Yes	Edent	Edent
13. F 44	No	Yes	1	Od	Well	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14. F 45	No	Yes	1	Od	Well	No	No	No	No	N/A	No	No

Case No. Gender & Age	Predominant radiodensity			Other Radiological features								
	Radio-lucent	Central Opacity	Number of Opacities	Shape	Margin Definition	Cortex Present (+sclerosis (S))	Expansion	Specific Anatomical Features		Inferior dental canal(IDC) Displaced?	Tooth Resorption	Tooth Displacement
15. F 48	No	Yes	1	Rd	Well	No	Yes	No	No	No	No	No
16. F 50	No	Yes	1+	Od	Well	No	Yes	No	No	No	No	No
17. F 52	No	Yes	1	Od	Well	No	Yes	No	No	N/A	No	No
18. F 52	No	Yes	1	Rd	Well	No	Yes	Yes	Yes	Yes	No	No
19. F 55	No	Yes	2	Od	Well	No	Yes	No	No	N/A	No	No
20. F 80	No	Yes	1	Od	Well	No	Yes	No	No	N/A	Edent	Edent

Abbreviations and Notes: d, IDC is displaced downward; edent, edentulous; INA, Information not available; Mult. Multilocular; N/A, not applicable-affected jaw was edentulous; [a]predominant pattern; [b]Indian origin; * shorter roots; u, IDC is displaced upward; Od. Ovoid; Rd, round

TABLE 6.3. Cemento-Ossifying Fibroma: Hong Kong Patients; Differential and provisional diagnosis

Case No. & *Histopath.*	Gender & Age(years)	COF	Cementoma	COD	FOL	Cemento-blastoma	CEOT	Odontoma	Other
Maxilla									
1. *OF*	F 18	**Yes**							
2. *OF*	F 26				**Yes**			**Yes**	
3. *OF*	F 30								***Nil***
4. *CF*	F 44				**Yes**				
Mandible									
1. *COF*	F 10	**Yes**						**Yes**	Other cal T
2. *CF*	F 21								***Nil***
3. *COF*	F 26	**Yes**	**Yes**	**Yes**			**Yes**		COC
4. *COF*	F 26								Ameloblast.
5. *CF*	F 28								***Nil***
6. *COF*	F 29								***Nil***
7. *COF*	F 33	**Yes**				**Yes**			
8. *COF*	F 35								***Nil***
9. *CF*	F 37					**Yes**			
10. *CF*	F 38								***Nil***
11. *COF*	F 39								***Nil***
12. *OF*	F 39								Osteomyelit.
13. *OF*	F 44	**Yes**	**Yes**				**Yes**		
14. *CF*	F 45								***Nil***
15. *CF*	F 48								***Nil***
16. *CF*	F 50				**Yes**				Osteroma

Case No. & *Histopath.*	Gender & Age(years)	COF	Cementoma	COD	FOL	Cemento-blastoma	CEOT	Odontoma	Other
17. *COF*	F 52	**Yes**							
18. *COF*	F 52				**Yes**				
19. *CF*	F 55					**Yes**			
20. OF	F 80	Yes						Yes	

Abbreviations and Notes: Ameloblast, Ameloblastoma; cal. T; calcified tumour; COC, calcifying odontogenic cyst; CF, cementifying fibroma; COF, cemento-ossifying fibroma; Histopath., histopathology; No., number; OF, ossifying fibroma; Osteomyelit, osteomyelitis.

Table 6.4. Cemento-Ossifying Fibroma: Hong Kong Patients; Follow-up and recurrence

Case No. & *Histopath.*	Gender & Age(years)	Follow-up?	Review Duration (years)	Discharge by Patient or Surgeon ?	Recurrence? (re-growth after surgery)	Recurrence with similar Histopathology?	Recurrence with similar Radiology?
Maxilla							
1. *OF*	F 18	Yes	16	F-U continues	No	-	-
2. *OF*	F 26	ING					
3. *OF*	F 30	Yes	2	Patient	No	-	-
4. *CF*	F 44	Yes	10	Patient	No	-	-
Mandible							
1. *COF*	F 10	Yes	7	F-U continues	No	-	-
2. *CF*	F 21	Yes	4	Patient	No	-	-
3. *COF*	F 26	Yes	2	Patient	No	-	-
4. *COF*	F 26	Yes	16	F-U continues	No	-	-
5. *CF*	F 28	No	-	Patient	ING	-	-
6. *COF*	F 29	Yes		F-U continues	Yes	same	same
7. *COF*	F 33	Yes	2	Patient	No	-	-
8. *COF*	F 35	ING					
9. *CF*	F 37	ING					
10. *CF*	F 38	No	-	-	ING	-	-
11. *COF*	F 39	Yes	6	Patient	No	-	-
12. *OF*	F 39	Yes	2	Patient	No	-	-
13. *OF*	F 44	Yes	6	Patient	No	-	-
14. *CF*	F 45	Yes	2		No	-	-
15. *CF*	F 48	Yes	0.6	Patient	No	-	-
16. *CF*	F 50	Yes	2	Patient	No	-	-
17. *COF*	F 52	ING				-	-

Case No. & *Histopath.*	Gender & Age(years)	Follow-up?	Review Duration (years)	Discharge by Patient or Surgeon ?	Recurrence? (re-growth after surgery)	Recurrence with similar Histopathology?	Recurrence with similar Radiology?
18. *COF*	F 52	No	-	Patient	ING	-	-
19. *CF*	F 55	ING					
20. OF	F 80	Yes	2	Patient	No	-	-

Abbreviations and Notes: CF, cementifying fibroma; COF, cemento-ossifying fibroma; F-U, follow-up; Histopath., histopathology; ING, information not given; No., number; OF, ossifying fibroma;

The overall mean size (area) of the 22 lesions, which could be measured from the radiographs (displaying a lateral projection of the COF – panoramic and periapical radiographs), was 4.77 (sd 3.73) cm^2. The mandibular cases were divided into 3 age groups; up to 30 by which age the peak bone mass has been achieved (6 cases (Mandibular Cases. 1 to 6); 6.87 sd 4.08 cm^2); 30 up to 50 years moderate constant decrease in bone mass (9 cases (Mandibular Cases. 7 to 15) reduced to 8 after removing the uncharacteristically large Mandibular Case 13; 1.95 sd 0.58 cm^2); 50 years upwards as the onset of menopause in Chinese women occurs just after 50 years (Loh and Yeo, 1989) with accelerated loss of bone mass (5 cases(Mandibular Cases. 17-20); 5.25 sd 2.76cm^2). The younger and older groups were significantly larger than the middle group ($t = 2.93$ (12df) and 2.64 (11df) respectively; $0.05 > P > 0.01$), whereas there was no significant difference between the youngest and oldest groups ($t = 0.81$; 9df; $P > 0.05$). There was also no significant difference between those cases detected incidentally and those with symptoms for any age group: $X^2 = 0.09$; 2df: $P > 0.05$.

COFs appeared radiographically as well-defined unilocular round or oval structures (Table 6.2.). The 16 mandibular and two maxillary COFs presented with central radiopacities (Figure 2). The remaining 2 maxillary cases presented as dense opacifications. The four radiolucent lesions occurred in the younger patients (32.25 sd 5.85, but not significantly so with regards the remaining 20 cases; 38.80 sd 15.81; $t = 1.43$; 22df; $P > 0.05$). According to Slootweg and Muller's (1990) objective test, all COFs possessed well-defined peripheries. In addition 11 cases had cortices, and

first presented in the third and fourth decades. Cortication of the periphery tends to be present in younger cases ($t = 2.03$; 18df; $P > 0.05$).

Nineteen lesions exhibited buccolingual expansion (Figure 2); in the mandible, it was present in all of the five oldest cases affecting the mandible and 5 of the youngest 6 cases whereas only 4 such cases were observed in the 9 middle-aged mandibular cases. The associations between non-expansion of the mandible and CFs (4 out of 6 non-expansions) and displacement of teeth and COFs (3 out of 4 tooth displacements) are not significant ($X^2 = 2.54$ and 1.81 respectively; 1df; $P > 0.05$). Table 6.2 displays the radiographic presentation revealed 4 radiolucencies, all of the COF subtype; this was significant ($X^2 = 9.54$; 3df; $0.05 > P > 0.01$). Those in the mandible presenting with central opacities, appeared to present with more than one in older patients; this not significant even with the 80 year old patient excluded ($t = 1.41$; 17df: $P > 0.05$).

Five mandibular lesions, (all in the posterior quadrant), presented with downward displacement of the inferior border of the mandible; three were also associated with its thinning (Figure 2). Eight out of 13 lesions (all 3 forms) in the posterior mandible displace the inferior dental canal. The 3 COFs sited in the posterior quadrant of the maxilla had expanded upwards into the maxillary antrum. Displacement and resorption of adjacent roots occurred in 6 and 1 cases respectively.

A provisional diagnosis was available in 15 cases (Table 6.3). Of the 7 cases where COF was considered in the provisional diagnosis, only in 2 cases was it

offered as the sole diagnosis (Maxillary No. 1. and Mandibular No. 17). Not a single case contained FD in its provisional or differential diagnosis.

The histopathological reports revealed 6 as OFs and 9 each as CFs and COFs. Three of the OFs were found in the maxilla and all 9 COF were reported in the mandible; these were significant ($X^2 = 8.4$; 2df; $0.05 > P > 0.01$). The 1.17-year difference between CF and OF (40.67 sd 10.86 and 39.50 sd 21.89 respectively) was not significant ($t = 0.12$; 13df; $P > 0.05$). The 7.11-year younger mean age of the COF subtype (33.56 sd 13.24) did not differ significantly from the CFs ($t = 1.24$; 16df; $P > 0.05$).

Follow-up and recurrence were detailed on Table 6.4. Sixteen cases were followed-up, 3 were not, and no comment was made on the remaining 5. Eleven patients discontinued follow-up after a mean of 3.51 years (sd 2.77). Only one recurred and displayed the same histopathology and radiology as at its first presentation.

B: Systematic review

Selection Criteria.

Many of the reports were automatically rejected because they were single case reports or review articles. Those excluded under specific exclusion criteria are set out in Table 6.5. There was no significant difference between the proportions of

English with non-English SR-excluded reports (Table 6.5.) with the SR-included reports for each of the 4 groups (Table 6.6.); $X^2 = 1.30$; 3df; $P > 0.05$.

Table 6.5. Cemento-Ossifying Fibroma: Excluded reports

Selection Criterion	Report (1st author's surname and date of publication)	Gp.	Language of Publication
2	Sobral et al. (2003)	L	Portuguese
1	Kuyama et al. (2000)	O	English
2	Barcelos et al. (1998)	L	Portuguese
1	Lu et al. (1998)	O	Chinese
A	MacDonald-Jankowski (1998)	O	English
1	Janah et al. (1997)	A	French
2	Su et al. (1997 a & b)	W	English
2	Bucket et al. (1994)	W	French
1	Ackermann & Altini (1992)	A	English
2	Nakade et al. (1989)	O	Japanese
1	Chomette et al. (1987)	W	French
1	Jammet et al. (1987)	W	French
1	Buchmann & Bienengraber(1986)	W	German
2	Wu & Chen (1985)	O	English
1	Zachariades et al. (1984)	W	English
1	Sweet et al. (1981)	W	English
1	Thompson (1981)	W	English
1	Khanna et al. (1980)	W	English
B	Boysen et al. (1979)	W	English
1	Shear & Rachanis (1979)	A	English
1	Regezi et al. (1978)	W	English
A	Eversole et al. (1972)	W	English
1	Panders (1970)	W	English
1	Chung et al. (1969)	O	English
2	Odeku et al. (1969)	A	English
1	Hamner et al. (1968)	W	English
1	Anand et al. (1967)	A	English
1	Pound et al. (1965)	W	English
2	Bhansali et al. (1961)	W	English

Abbreviations: A, African; L, Latin-American; O, Oriental; W, Western.

Criterion 1:

Seventeen reports were excluded under 'Criterion 1.' Generally reports earlier than 1970 were not readily included by 'Criterion 1' because they deviated from the current histological definition of COF. Many of these reports were derived from general or medical pathological rather than oral and maxillofacial pathological sources and therefore were more likely to be rejected unless they expressed a clear understanding that the FD and COF, having the similar range of histopathological FOL appearances, can only be distinguished by radiology; the former has a poorly-defined margin, whereas the latter has a well-defined margin. Although Khanna and co-authors (1980) did make reference to Waldron and Giansanti's (1973b) report, their study was excluded because its text left the clear impression that they considered FOL to be a synonym of COF. Also they did not consider FD or the role of radiology; since this is purely a histopathological report.

Another important diagnostic dilemma, as observed in Chapter 5, is that between COF and FocCOD. Hamner and co-authors' (1968) report was excluded because it was not possible to identify the COD cases and exclude them.

The COF encompasses the entire histopathological spectrum from completely osteoid (OF-like) to completely cementoid (CF-like). Some reports, such as Eversole and co-authors (1985a and b), use OF when clearly meaning COF, Matsuzaka and co-authors (2002) reported 65 cases as FOLs, which is not a diagnosis and were excluded from further consideration. Although Sweet and co-authors (1981) referred

to the WHO's first edition and Waldron and Giansanti (1973b), it was very clear that the authors meant only to confine their review to CF, excluding OF and COF. Ackermann and Altini (1992), Regezi and co-authors' (1978), and Kuyama and co-authors' (2000) reported only CFs. Iwasa and Soda (1980) reported their 24 cases with sufficient detail that the 9 multiple cases were identified and removed.

The reports by Obwegeser and co-authors (1973), Talbot and co-authors (1974), and Garau and co-authors (1997) clearly included COFs and reported them in sufficient detail to allow them to be identified and removed. Nevertheless, such COFs could not be included in the COF SR, because they were unlikely include all COFs observed within that community for that particular period. Furthermore, because they were primarily FD reports, they were not entered among the excluded COF reports in Table 6.5.

Criterion 2.

Eight reports were excluded under 'Criterion 2.' Bhansali (1961) reported that only a third of his cases as well-defined. Su and co-authors (1997a and b) reported that 15% of their COFs were poorly-defined with regards to focal CODs. There was no discussion of this inconsistency with reference to FD. Furthermore, the reproduction of some of their radiographs was so poor (particularly those which purported to display examples of poor-defined margins, and then only those in relation to CODs) that their criterion as to what constituted such a margin was unclear. Therefore, their study had to be excluded from this SR. Although Wu and

Chan (1986) cited the WHO's first edition and reported OF and CF separately no comment was made with regards to their radiology; this report was excluded. Of Iwasa and Soda's (1980) 15 remaining cases, the 3 poorly-defined cases were identifiable and removed allowing the remainder to be included in the SR.

Although reporting 64 cases, Eversole and co-authors (1985a) could only retrieve the radiographs of only 43; the inclusion of the remaining 19 was based solely on the entries of well-defined margins in the patients' journals by the attending clinicians. This acceptable and their report was included. As only 10% of Waldron and Giansanti (1973b) cases were poorly-defined, their report was included.

Zhou and co-authors (1989) reported OF and CF cases which were included, but also osteofibroma (extragnathic COF; see Schajowicz, 1993) which was not included primarily because Zhou and co-authors (1989) did not include it in their radiological descriptions.

Criterion 3.

No reports were excluded under this criterion. Jones and Franklin's two studies (2006a and b) were based on the same community, one of children and one of adults; the results of both were combined and included.

Criterion A:

Two reports were excluded under 'Criterion A.' The report by MacDonald-Jankowski (1998) is contained within the present series study and SR; Eversole and co-authors (1985) must have included those COFs which Eversole and Rovin reported in 1972; the latter report was therefore excluded. On the other hand Yamamoto and co-authors (1985) reported the same material as Sakato (1977b), but because they added more detail which complemented, but did not replace Sakato's (1977b report, Yamamoto and co-authors' (1985) report was included under Sakato (1977b).

Criterion B.

The report by Boysen and co-authors (1979) was excluded under this criterion.

Criterion C.

No reports were excluded under this criterion.

The present study and the SR

Twenty-seven reports of series of cases, including the present study, were included in the SR. There is no statistical difference between the proportion of English-language published reports for the 26 included reports (Note: the present study although included is excluded from this comparison) in Table 6.6; and the 27

excluded reports (Table 6.5); $X^2 = 0.03$; 1df; $P > 0.05$. The clinical features, decades at first presentation, histopathological presentation and radiological details extracted from each of the series are distributed in Tables 6.6, 6.7, 6.8, and 6.9 respectively. A synthesis of the 26 already published and SR-included series is compared statistically to the present study in Table 6.10.

In Map 6.1 the 'Western' group included 11 reports came from North America and Europe (including 1 from India); the 6 African reports (including 1 from Jamaica); 8 Oriental reports (including the present study); and 2 Latin-American reports. Furthermore, non-Whites, particularly Blacks were well represented in 'Western' reports, especially in that by Waldron and Giansanti (1973b).

The 'number of COFs per hospital per year' was displayed in Table 6.6. The 'number of COFs per hospital per year' was not determinable for 7 reports. The 'number of COFs per hospital per year' also fell from 2.44 (sd 2.0) prior to 1990, to 1.2 (sd 1.2) COFs per year from and including 1990; this was not significant ($t = 1.63$:17df: $P > 0.05$).

Most reports included the patients' sex, age and site affected, but only 9 included any presenting clinical details (Table 6.6). Eight reports considered whether their cases did or did not recur after treatment, only 2 were published since 1990. The SR's recurrence rate was 6.0%; the difference between the present study and the SR was insignificant. Table 6.10 reveals only 3 significant differences between the

present study and the rest of the SR; the Hong Kong study's exclusive predilection for females, proportionally fewer cases presenting with swelling or root resorption. The mean age at first presentation of the Hong Kong Chinese was 38 years, higher than that of the SR's mean of 31 years.

The patients' pre-presentation awareness of their lesions was recorded or determinable only in two reports, the present study and that by Agrestini and co-workers (1987). The mean was 0.8 years.

Table 6.7 displays a comparison between reports of the distribution according to age in decades. Most of the cases occur in the 3rd and 4th decades. Males predominate in the first decade, whereas the females increasingly predominate from the second to the 5th decades; the proportion of males increases in the 6th decade, but females still predominate. This pattern is consistent in all reports with 18 or more cases. The males in Table 6.7 account for 23% in contrast to 28% in the SR (Table 6.6); this is significant ($X^2 = 9.80$: 1df: $P < 0.001$).

Three subtypes of COF have been described; they are CF, OF and COF and are set out in Table 6.8, which displays a synthesis of two reports and the present study. This shows that the OF form predominates in the first 3 decades, and the CF in the next 3 decades; the latter is absent in the last 2. The significant difference between the 3 subtypes ($X^2 = 7.52$: 2df: $0.05 > P > 0.01$) with regards to gender substantially enhances the possibility for the phenomenon reported in the preceding paragraph is the very few males with the COF subtype.

Table 6.6. Cemento-Ossifying Fibroma: Systematic review; Analysis of the included reports.

First Author (year)	National and/or Ethnic origin (Number of Hospitals(H) and number of Cities(C))	Period covered	No. of COF (No. per hospital per yr)	Gender Males Females	Age mean (range) in years / Pre-Presenting duration mean(range) in years	Presenting Signs & Symptoms: Swelling	Pain	Other	SITE: Mandible Ant.Post.	Maxilla Ant. Post.	Comments / Follow-up (FU) and Recurrence
Schmaman (1970)	Sth African (All B) (1H:1C)	13 years	26 (2.0) *9CF* *11OF* *6COF*	ING*	ING(12-38) for OF only *ING*	ING*	ING*	ING	16 *5CF* *6OF* *5COF*	10 *4CF* *5OF* *1COF*	* At least 1 OF is a F with pain & swell 5 FDs FU 2 recur
Waldron (1973)	US (12W;21B#) (1H:1C)	1957-1971 14 years	43 (3.1) *15CF* *19OF* *8COF*	7 36#	ING(15-70) *IIG (0.5-10)*	13	4	24*Incid 2 numb	37	0 6	**majority* # All B are F FU ING
Kawai (1974)	Japanese (1H:1C)	20 years	18 (0.9) *10CF* *8OF*	ING	ING *ING*	ING	ING	ING	ING	ING	 FU ING
Langdon (1976)	UK(9W;1B*) (1H:1C)	1966-1975 10 years	10 (1.0)	3* 7	**35**(ING) *IIG*	ING	ING	ING	1 6	2 1	* now mand, 9 yrs ago bilat max FU ING

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Males Females	Age	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Sakato (1977)	Japanese (1H:1C)	ING	28 *17CF* *11OF*	9 19 *6 CF 11* *3 OF 8*	**32**(7-12) *CF 34 (12-72)** *OF 29 (7-47)** *ING*	27 *16CF* *11OF*	3 *2CF* *1OF*	0 Incid.	23 *14CF** *9OF**	5 *3CF** *2OF**	* Modified by Yamamoto FU ING
Adekeye (1980)	Nigerian (1H:1C)	1 year	7 (7.0)	3 4	**14**(6-29) *2.6(0.4-10)*	7	0	2 teeth displ & 2 exfoliated 0 Incid.	4	3	5 FDs 0 recur
Iwasa (1980)	Japanese (1H:1C)	1960-1979 19 years	12 (0.6)	3 9	**34**(6-47) *ING*	10	2	1 Incid.	0 (11) 10	0 1	 1 recur
Ajagbe (1983)	Nigerian (1H:1C))	1966-1980 15 years	27 (1.8)	9 18	**22**(IIG) *ING*	IIG	IIG	IIG	12	15	 10%FU 5yr
Eversole (1985)	US (50%W; 16%B;21%H ;10%O;3%A) (1H:1C)	ING	64	12 52	**36** *ING*	IIG Few swelling, majority incidental			46 11	4 3	Radiology for 43 cases 23FUmean3yr 5 recur
Rados (1986)	Chilean (1H:1C)	ING	12 *6 CF* *6 OF*	3 9 *3 CF 3* *0 OF 6*	33 (10-59) *CF 36 (17-49)* *OF 30 (10-59)* *ING*	ING	ING	ING	2 8 *1 CF 4* *1 OF 4*	0 2 *0 CF 1* *0 OF 1*	 FU ING

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Males Females	Age	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Agrestini (1987)	Italian (1H:1C)	ING	6 *2CF* *4OF*	4 2 *1 CF 1* *3 OF 1*	**28**(11-56) *CF 39 (25-53)* *OF 22 (11-56)*	3	3	0 Incid.	4 *1CF* *3OF*	2 *1CF* *1OF*	
					0.9(0.25-2)						1 recur
Cossi (1987)	Italian (1C:1H)	ING	3	2 1	**38**(16-50)	1	0	3 incid 1UE	0 1	1 1	
					ING						FU ING
Sciubba (1989)	US(14W; 2B: 2H) (1H:1C)	1967-1987 20 years	18 (0.9)	7 11	**30**	ING	ING	ING	3 11	1 3	
					ING						FU 1-21 yr 1 recur
Van Heerden (1989)	Sth African (maj B) (1H:1C)	6 years	30 (5.0)	ING	ING	ING	ING	ING	ING	ING	
					ING						FU ING
Yoon (1989)	Korean (1H:1C)	1977-1986 10 years	16 (1.6)	4 12	ING(0>69)	13	2	1NG	2 9	2 3	
					IIG (0.02-20)						FU ING
Zhang (1989)	Chinese (1H:1C)	ING	15	11 4	ING(10-50)	ING	ING	ING	11	4	
					ING						FU ING
Zhou (1989)	Chinese (1H:1C)	1966-1985 20 years	29 (1.4) *15CF* *14OF*	ING	IIG	ING	ING	ING	IIG	IIG	
					ING						FU ING
Slootweg (1990)	Dutch(ING) (1H:1C)	ING	12	8 4	**25**	ING	ING	ING	7	5	
					ING						FU ING

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Males Females	Age	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Swaroop (1990)	Indian (1H:1C)	1963-1981 18 years	8 (0.4) *5CF* *3OF*	ING	ING	8	IIG	0 Incid.	IIG	IIG	4-7cm in size
					IIG(0.1-6)						FU ING
Summerlin (1994)	US(27W; 10B;8?) (1H:1C)	ING	45	15 30	**30**	IIG Frequently painless swelling			32	13	Site unknown for 2 cases
					ING						FU ING
Mosqueda-Taylor (1997)	Mexican (4H:1C)	1960-1996 36 years	5 (0.03)	ING	ING	ING	ING	ING	0 1	1 3	
					ING						FU ING
Stypulkowska (1998)	Polish (1H:1C)	1956-1996 40 years	11 (0.3)	IIG	IIG	ING	ING	ING	IIG	IIG	
					ING						FU ING 2 recur
Ogunsalu (2001)[a]	Jamaican (2H:1C)	1980-1995 15 years	8 (0.5)	2 6	**22**(10-47)	ING	ING	ING	1 2	2 (5) 2	Ant&post affect 1 max
					ING						FU ING
Matsuzaka (2002)	Japanese (1H:1C)	1966-2001 35 years	134(3.8) *49 CF* *60 OF* *25 COF*	35 99 *12 CF 37* *20 OF 40* *3 COF 22*	**30**[a] CF; c30.0 (>10-<59) OF; 30.4 (>0-<69)	ING	ING	ING	IIG	IIG	38 cementomas
					ING						FU ING
Simon (2002)	Tanzanian (national)	1982-1997 15 years	30 (2.0) *2CF* *28 OF*	ING	ING	ING	ING	ING	ING	ING	2CF in Mand-1M&1F
					ING						FU ING

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	(No. per hospital per yr)	Males Females	Age	Swelling	Pain	Other	Mandible Ant.Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Jones (2002)	UK (1H:1C)	1973-2002 30 years	33(1.1)*	8* 25*	**37*** (ING) *ING*	ING	ING	ING	ING	ING	* included children FU ING
Present (2006)	Hong Kong (100%O) (1H:1C)	1982-2004 22 years	24 (1.1) *9 CF* *6OF* *9COF*	0 24 0 CF 9 0 OF 6 0 COF 9	**38**(10-80) *CF(21-50)* *OF(18-80)* *COF (10-52)* *0.7(0-10)*	8 *2CF* *2OF* *4COF*	3 *0CF* *2OF* *1COF*	14 incid *6CF* *4OF* *3COF* 1 loose tth *1COF*	6 (20) 12 *(2 COF)** *4 CF 4* *1 OF 2* *1 COF 6*	1 3 *0 CF 1* *1 OF 2*	* both affect post. & ant. Sextants AND 1 crosses the midline FU 0 recur
Total number of cases			674	145[b] 372[b]	31[c]6-80) *1.1*[d]*(0-6)*	80[e]	17[f]	42 Incid[g]	282[h] 61[i] 71[i]	102[h] 14[i] 28[i]	12[j] recur
Percent of cases				28 72		54	12	31	73[h] 46[i] 54[i]	27[h] 33[i] 67[i]	6
Total number of series			(19)[a]	19	16[c] (210 *3*[d] *(5)*	9	8	8	19[h] and 10[i]		8
Percent of 27 series			(70)	70	59[c] (78) *11*[d] *(18)*	30	30	30	70[h] and 37[i]		30

Abbreviations and Notes: [a], this mean could only be calculated from CF and OF values, but not from COF which had none; ant, anterior; B, Black; C, City; CF, Cementifying fibroma; FU, Follow-up; H, Hospital; O, oriental/ East Asian; OF, ossifying fibroma: IIG, inadequate information given; ING, Information not given; Incid, incidental finding; NO. Nasal obstruction; post. posterior; recur, recurrences; tth. Teeth; W, White/Caucasian; yr, year/s

Key	Number of reports	Total number of cases
a. No.COF/H/yr	19	489
b. Gender	19	517
c. Mean Age	16	443
d. Awareness	3	37
e. Swelling	9	147
f. Pain	8	139
g. Incidental	8	131
h. Site: Jaw	19	384
i. Site:Ant./Post	10	Md:133; Mx: 42
j. Follow-up/ Recurrence	8	199

Table 6.7. Cemento-Ossifying Fibroma: Systematic review; Distribution of cases according to age (in decades). *The number of males and females are in parentheses*

Report Decade	Adek-eye	Ajag-be	Eversole	Rados	Sciubba	Yoon	Summ-erlin	Matsu-zaka	Total of earlier Reports	Present Study	Overall Total	Decad. % of Total	% of Males/ Decad.
0-9	2(1:1)	5	1(1:0)	0	1(1:0)	1	1	3(1:2)	14(4:3)	0	14(5:3)	4	**57**
10-19	4(2:2)	8	8(2:6)	3(0:3)	5(2:3)	5	9	20(13:7)	62(19:22)	2(0;2)	63(19:23)	18	**45**
20-29	1(0:1)	3	18(4:14)	3(1:2)	3(1:2)	3	15	28(6:22)	74(12:41)	6(0:6)	80(12:47)	23	**20**
30-39	0	8	18(2:16)	1(0:1)	3(1:2)	2	8	37(7:30)	77(10:49)	7(0:7)	84(10:56)	25	**15**
40-49	0	1	8(1:7)	3(2:1)	4(1:3)	3	6	24(5:19)	49(9:30)	4(0:4)	53(9:34)	15	**21**
50-59	0	1	8(0:8)	2(0:2)	1(0:1)	0	3	17(2:15)	32(2:26)	4(0:4)	36(2:30)	11	**6**
60-69	0	1	3(2:1)	0	1(1:0)	2	0	5(1:4)	12(4:5)	0	12(4:5)	4	**44**
70-79	0	0	0	0	0	0	0	0	0	0	0	0	**0**
80-89	0	0	0	0	0	0	0	0	0	1(0:1)	1(0:1)	0	**0**
Total	7(3:4)	27	64(12:52)	12 (3:9)	18(7:11)	16	42	134(35: 99)	320 (60:175)	24(0:24)	344 (60:199)	100	23

Table 6.8. Cemento-Ossifying Fibroma: Systematic review; Distribution of the 3 histological presentations according to age (in decades).

The number of males and females are in parentheses

Decade & Histopath.	Report	Yoon	Matsuzaka			Present Study			Matsuzaka & the Present Study			ALL	Percentage of males/decade/ each presentation		
			M	*F*	ALL	*M*	*F*	ALL	*M*	*F*	ALL				
0-9	CF	1	*0*	*0*	0	*0*	*0*	0	*0*	*0*	0	1	25	CF	0-9
	OF	0	*1*	*2*	3	*0*	*0*	0	*1*	*2*	3	3	75	OF	
	COF	0	*0*	*0*	0	*0*	*0*	0	*0*	*0*	0	0	0	COF	
10-19	CF	0	*4*	*2*	6	*0*	*0*	0	*4*	*2*	6	6	22	CF	10-19
	OF	3	*7*	*5*	12	*0*	*1*	1	*7*	*6*	13	16	59	OF	
	COF	2	*2*	*0*	2	*0*	*1*	1	*2*	*1*	3	5	18	COF	
20-29	CF	0	*3*	*6*	9	*0*	*2*	2	*3*	*8*	11	11	30	CF	20-29
	OF	3	*3*	*13*	16	*0*	*1*	1	*3*	*14*	17	20	54	OF	
	COF	0	*0*	*3*	3	*0*	*3*	3	*0*	*6*	6	6	16	COF	
30-39	CF	1	*4*	*12*	16	*0*	*2*	2	*4*	*14*	18	19	42	CF	30-39
	OF	0	*3*	*10*	13	*0*	*2*	2	*3*	*12*	15	15	31	OF	
	COF	1	*0*	*8*	8	*0*	*3*	3	*0*	*11*	11	12	27	COF	
40-49	CF	1	*1*	*9*	10	*0*	*3*	3	*1*	*12*	13	14	45	CF	40-49
	OF	2	*3*	*6*	9	*0*	*1*	1	*3*	*7*	10	12	38	OF	
	COF	0	*1*	*4*	5	*0*	*0*	0	*1*	*4*	5	5	16	COF	
50-59	CF	0	*0*	*8*	8	*0*	*2*	2	*0*	*10*	10	10	48	CF	50-59
	OF	0	*2*	*2*	4	*0*	*0*	0	*2*	*2*	4	4	19	OF	
	COF	0	*0*	*5*	5	*0*	*2*	2	*0*	*7*	7	7	33	COF	
60-69	CF	0	*0*	*0*	0	*0*	*0*	0	*0*	*0*	0	0	0	CF	60-69
	OF	1	*1*	*2*	3	*0*	*0*	0	*1*	*2*	3	4	57	OF	
	COF	1	*0*	*2*	2	*0*	*0*	0	*0*	*2*	2	3	0	COF	

Decade & Histopath.	Report	Yoon	Matsuzaka			Present Study			Matsuzaka & the Present Study			ALL	Percentage of males/decade/ each presentation		
			M	*F*	ALL	*M*	*F*	ALL	*M*	*F*	ALL				
70-79	CF	**0**	*0*	*0*	**0**	*0*	*0*	**0**	*0*	*0*	**0**	**0**	0	CF	70-79
	OF	**0**	*0*	*0*	**0**	*0*	*0*	**0**	*0*	*0*	**0**	**0**	0	OF	
	COF	**0**	*0*	*0*	**0**	*0*	*0*	**0**	*0*	*0*	**0**	**0**	0	COF	
80-89	CF	**0**	*0*	*0*	**0**	*0*	*0*	**0**	*0*	*0*	**0**	**0**	0	CF	80-89
	OF	**0**	*0*	*0*	**0**	*0*	*1*	**1**	*0*	*1*	**1**	**1**	0	OF	
	COF	**0**	*0*	*0*	**0**	*0*	*0*	**0**	*0*	*0*	**0**	**0**	0	COF	
	TOTAL	**16**	**35**	**99**	**134**	**0**	**24**	**24**	**35**	**123**	**158**	174	**22**		

Table 6.9. Cemento-Ossifying Fibroma: Systematic review; Analysis of the radiology in the included reports.

Radiological Features / Author (year)	No of cases	Predominant Radiographic Presentation			Shape			Corti-cation of Peri-phery	Expansion						Tooth Displace-ment		Root Resorp-tion	
		Radiopacity							Bucco-lingual		Lower Border of the Mandible displaced (and/eroded)		Antral Involvement					
		Radio-lucency	within Radio-lucency	Opaque	Oval	Round/ Spherical	Multi-locular		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Schmaman (1970)	26	0	26	0	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING
Waldron (1973)	43	11	27	5	ING	ING	ING	23	ING	ING	ING	ING	IIG	IIG	ING	ING	ING	ING
Adekeye (1980)	7	3	2	2	ING	ING	ING	ING	7	0	4	0	2	1	1	6	1	6
Eversole (1985)	43	21	18	4	*36 [c] unilocular*		3	ING	IIG	IIG	ING	ING	ING	ING	11	32	7	36
Agrestini (1987)	6	1	3	2	ING	ING	ING	ING	ING	ING	1	3	ING	ING	1	6	ING	ING
Cossi (1987)	3	0	3	0	ING	ING	ING	ING	*1 [c]*	ING	ING	ING	1	0	ING	ING	ING	ING
Scuibba (1989)	18	10	7	1	ING	ING	*1 [c]*	ING	13	5	ING	ING	3	0	6	12	8	10
Zhang	15	2	1	12	ING	ING	ING	14	IIG	IIG	ING	ING	IIG	IIG	11 [b]	7	7	8
Swaroop	8	2	1	5	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING
Ogunsalu(1998)	8	1	4	3	*1 [c]*	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING
Present	24	4	18	2	11	9	2	11	19	5	5	7	3	0	6	18	1	23
Summary	201	55	110	36	11/24	9/24	5/67	48/82	39	10	10	10	9	1	36	81	24	83
Percent		27%	55%	18%	46%	38%	7%	54%	80%		50%		90%		31%		22%	
		Percent of 201 cases																

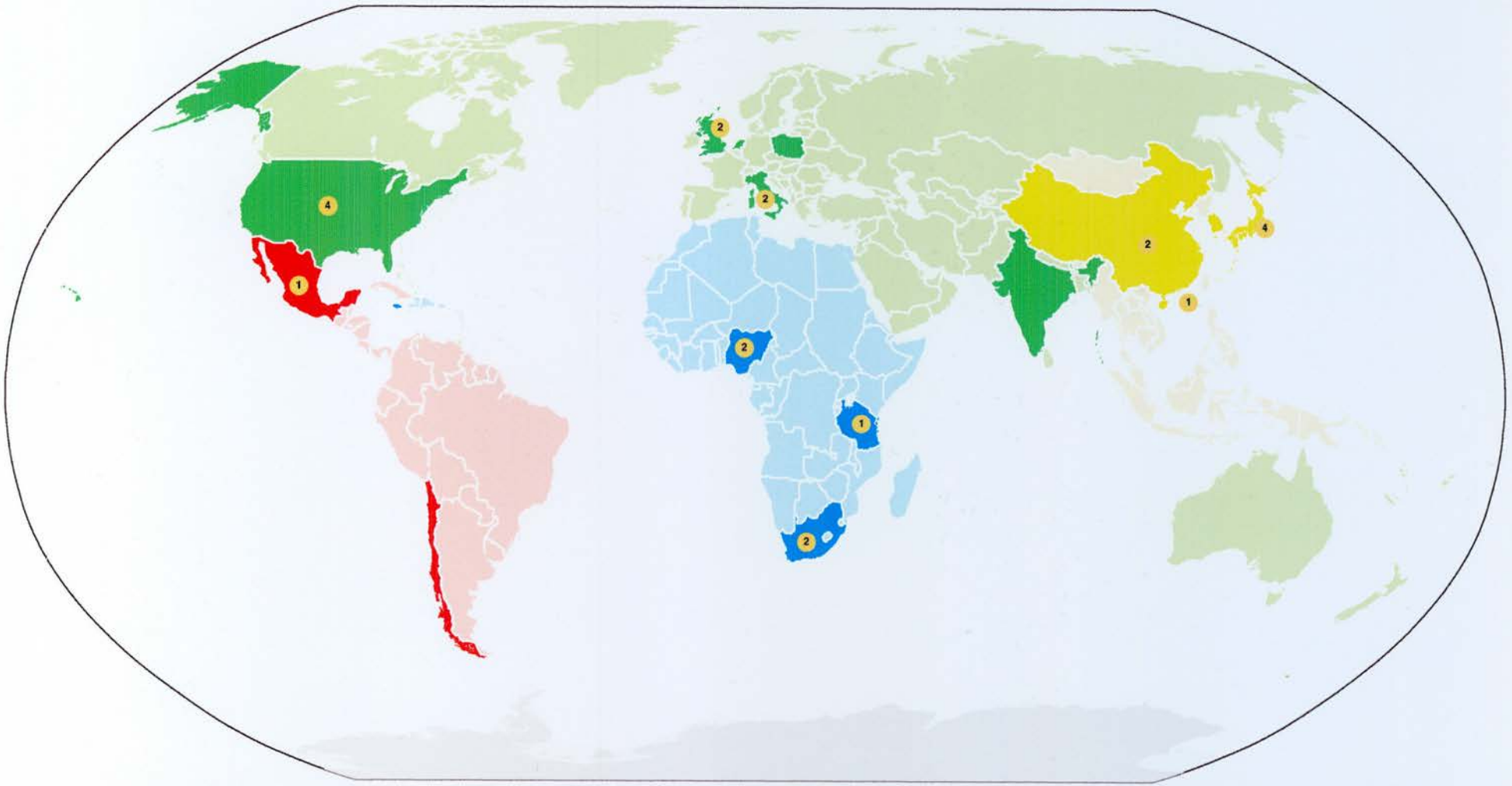
Abbreviations and Notes: [a], 16 cases which displayed either ground glass OR peau d'orange; [b], included 3 cases of exfoliated teeth; [c], Numbers in italics are not included in the calculations; C, cotton-wool; Cy, cyst-like; IIG, Inadequate information given; IIG*, If displacement occurred it was not marked; ING, Information not given; m, mottled; mi, mixed; Multiloc., multilocular; N/A, Not applicable; op, opacification of antrum or to varying degrees; p. pagetoid; w, whorled.

Cemento-Osseous Fibroma: Mandibular Case 13.

Note:Well-defined periphery with a translucent space.
Root resorption and tooth displacement
Displacement of inferior dental canal & displacement and thinning of the lower border of the mandible.
The central opacity displays some peau d'orange and cotton wool-like sclerosis

Figure 2.

Fig. 2



Map 3. Cemento-ossifying Fibroma: Global distribution of 27 Systematic Review-included series of cases coloured according to group

Map 3

There were no significant differences in the distribution of the 3 predominant presentations (Table 6.9) between the present study and the SR ($X^2 = 4.64$; 2df; $P > 0.05$). Figure 2 displays a classical case of COF, which is resorbing and displacing teeth and other adjacent structures. It is also very well-defined.

Table 6.10. Cemento-Ossifying Fibroma: Chi-square statistics

Feature	Hong Kong	Rest of SR	X^2	Deg. free	P
Gender:Male:Female	0:24	145:348	9.75	1	< 0.001
Jaw: Mandible:Maxilla	20:4	261:97	1.31	1	> 0.05
Swelling:Yes:No	8:16	82: 41	9.42	1	< 0.001
Pain: Yes:No	3:21	13: 102	0.02	1	> 0.05
Incident.Find:Yes:No	14:10	28:30	0.68	1	> 0.05
Recur:Yes:No	0:24	12:163	0.20	1	> 0.05
Predom.Radio.Present.	4:18:2	51:92:34	3.41	3	> 0.05
Multilocular:Yes:No	2:22	3:40	0.03	1	> 0.05
Cortication: Yes:No	11:13	37:21	2.18	1	> 0.05
Expansion:Yes:No	19:5	20:5	0.00	1	> 0.05
LowBord.Mand:Yes:No	5:7	5:3	1.00	1	> 0.05
AntralInvolve:Yes:No	3:0	6:1	0.45	1	> 0.05
ToothDisplace:Yes:No	6:18	30:63	0.48	1	> 0.05
RootResorpt:Yes:No	1:23	23:60	6.26	1	0.05> P >0.01

Abbreviations: Assoc w teeth, associated with teeth; Incident.Find, incidental finding; Dg.Fre, degrees of freedom; LowBord.Mand, lower border of the mandible; Predom.Radio.present, predominant radiological presentation; RootResorpt root resorption /displacement; SR, systematic review; ToothDisplace, tooth displacement.

Location of the lesions by quadrant or sextant was specified in 10 reports (Table 6.6). Although there was no difference between the present study and the SR ($X^2 = 2.05$; 3df; $P > 0.05$), the greatest predilection for the anterior mandible in Western reports in contrast to the posterior mandible in Oriental reports ($X^2 = 23.80$; 3df; $P < 0.001$); the difference between Latin-American and Oriental reports was insignificant ($X^2 = 3.06$; 3df; $P > 0.05$). Although the Africans were represented by

only 1 small Jamaican report (Ogunsalo et al, 2001), Blacks were well represented in most Western reports.

Table 6.10 reveals that the Hong Kong Chinese present with significantly less swelling at first presentation. Their predisposition for females is significantly greater than that for the rest of the SR. They also present with significantly less root resorption.

DISCUSSION

The selection criteria did exclude one large report, that by Su and co-authors (1997a and b). They reported 15% of their COFs had poorly-defined margins, which exceeded the 10% limit for inclusion in the SR. Furthermore, 10% of their COFs were presented as multiple small fragments similar to focal CODs, and in contrast to the large single enucleated specimen for the majority of COFs. This raises the possibility that many of the poorly-defined cases they report as COFs could be CODs; this report had to be excluded from the SR.

One possible reason why the mean age in the present study is higher than that of the SR, may be due to its complete absence of males. Sakota (1977b) observed that males first presented nearly 5.71 years younger than females (28.43 and 34.14 years respectively). Furthermore, Sakota (1977b) observed that OFs presented 4.62 years younger than CFs, which did not agree with Matsuzaka and co-authors (1997) reporting near equality at about 30 years. The present study reflects some elements of

these Japanese reports in that although CF was older it was only 0.66 years older; the mean age for both was about 40 years. Furthermore, the present study also included the COF subtype with a mean age of 34 years.

The fall in the 'number of COFs per hospital per year' before and after 1990 may be in part due to the establishment of formal oral maxillofacial surgical services globally, which substantially reduced the reservoirs of this disease. Black communities have the highest 'number of COFs per hospital per year', which reflects this. These will be further discussed in a subsequent chapter.

The exclusive preponderance of females in this series is not only an extreme case of this trend, but more specifically confirms the high female predilection in the only other report on this Hong Kong Chinese population by Wu and Chan (1986) which had been excluded from the SR under 'Criterion 2'.This predilection for females is statistically significant when compared with the 31 %: 69% male: female ratio seen in the other 493 non-Hong Kong cases (Table 6.10.). The complete absence of males in this series may be explained by reference to Table 6.7. The percentage of males falls from 51 % and 45 % for the first and second decades respectively to 20% and 15% for the third to fourth decades. In contrast 20 cases in this report occurred in the third decade and above, older than the decades within which males would be most likely found. Furthermore, in the earlier report on this community (MacDonald-Jankowski, 1998) it was suggested that the absence of COF in younger patients of either gender may be due to the early lesions having been misdiagnosed as periapical lesions or early (radiolucent) stage odontomas. The

additional 4 cases did add a 10 year old, which adds some weight to this earlier supposition. The earlier lesions may have been observed and treated separately by the schools dental service as a periapical lesion with no referral of the specimen for histopathology.

Although COF has the highest mean ages in Oriental communities, Blacks have both the lowest mean ages and the highest 'number of COFs per hospital per year'. This would suggest that COFs have both the highest predilection for Blacks and make themselves readily known to the patients so that they can seek early treatment, but the latter is not borne out by reviewing the presenting signs and symptoms. Only the report by Adekeye and co-authors (1980) reported 100% presentation of swelling but none with pain, a powerful inducer to seek prompt treatment.

The significant lower incidences in the present study for swelling in contrast to the rest of the SR could only reflect the fact that very few reports reported presenting complaints at all. This is put into a more realistic scenario by there being no significant difference between the present study and the rest of the SR for incidental findings, which necessarily not only excludes pain and swelling, but also all other lesser complaints. In the present study, the middle age group (30 to 49 years of age) displayed expansion significantly less frequently than the younger group (X^2 = 4.0; 1df: $P > 0.05$) and this less frequent expansion tending to significance with regard to the older group. $X^2 = 3.44$; 1df; $P > 0.05$). Therefore, the significantly lower proportion of swellings at first presentation may be a product of there being

proportionally fewer younger patients who may be most likely to present with symptoms in many of the other reports. Nevertheless, it can be seen from Table 6.6 that the clinical presentation is variable; almost all 28 individuals in Sakato's (1977b) Japanese series presented with swelling, and 3 with pain (similar to the present study), whereas over half of the individuals in Waldron and Giansanti's (1973b) American (inner-city/urban) population were symptom-free and therefore their lesions were discovered incidentally. This difference in presentation between the Orient and the West in the 1970s may have reversed by the 1990s; Eversole and co-authors (1985a and b) reported that the majority were still found incidentally, but by the 1990s Summerlin and Tomich (1994) were reporting that the majority were then painless swellings whereas the majority in the present report are found as incidental findings. This could indicate changes in the availability of health care and prosperity between Oriental and American communities. Although discovery of a lesion as an incidental finding suggests that it is not yet large enough to produce symptoms which may imply more frequent dental visits. This is not in agreement with adult Hong Kong dental patient conduct outside the school system as discussed in the introduction.

Of the 175 cases, 38% affected the anterior and 40% the posterior mandibular sextants, whereas 8% and 16% affected the respective maxillary sextants. The present study differed in that 27% affected the anterior and 54% the posterior mandibular sextants and 4% and 14% the respective maxillary sextants; the difference was not significant ($X^2 = 2.17$; 3df; $P > 0.05$).

The radiographic features of COF reported in the literature vary markedly (Table 6.9). The majority of those in the present report were mixed density lesions, whereas most of those described by Sciubba and Younai (1989) were radiolucent. A reason for this difference may be that the mean age of the cases in the latter report was younger than in the present study. The radiological appearance of the COF depends upon its maturity. Table 6.9 (read with mean ages in Table 6.6) would appear to confirm this; the study with the youngest mean age reports a higher proportion of radiolucent lesions, whereas the present report with the oldest mean age recorded the lowest. Furthermore, the appearance of complete radiolucencies only in the younger cases suggests that calcification will occur increasingly with age. The absence of radiolucencies in the oldest group in the present report may suggest that the larger size and expansion of COFs may reflect reactivation of COFs that pre-existed the onset of menopause, rather than *de novo* lesions.

Table 6.9 also shows that while all of COFs have radiographically well-defined borders, this feature was accompanied by marginal sclerosis and a thin cortex in only half of these cases. Table 6.2 shows that cortication is found in the third and fourth decades. Its presence is usually taken as indicative of a slow growing or relatively static lesion. Therefore, the absence of such a feature in the older patients suggests that these may be growing more rapidly. Therefore, if such growth occurs then it is more likely to present with symptoms.

Eighty percent of the cases in this study had bucco-lingual expansion, consistent with the 72% reported by Sciubba and Younai (1989). Vertical expansion

was also seen in the present report. The downward displacement of the lower border of the mandible, seen in 42% of cases in the present study, has not previously been reported. Ninety percent of COFs show expansion into the maxillary antrum (Table 6.9.). This overall value was derived from the present study and from Sciubba and Younai (1989) the only other larger report to specify this feature, in addition to the smaller reports by Adekeye and co-authors (1980) and Cossi and co-authors (1987). Antral involvement can on occasion be very substantial; Sciubba and Younai (1989) reported two cases, which reached the floor of the orbit.

Although the smaller size of the lesions in women in their mid-40s was unexpected, this difference may disappear with the reporting of more cases. The difference between the middle- and older-aged groups approached significance. This would suggest that COFs may arise as suggested by the radiolucent stages in the young age group, or their growth may be reactivated, in middle-to-old age. Further support for this notion is derived not only from the absence of cortification in the old aged patients, but also from the distribution of buccolingual expansion with age. Buccolingual expansion was most prevalent in the oldest group (the five cases over 50 years of age) but least in the middle group (between 30 and 50 years of age), whereas it was intermediate in prevalence in the five youngest (below 30 years of age). These features suggest that a hormonal change could be responsible for triggering the growth of COFs in later life. This effect has been considered for the growth of fibrous dysplasia in pregnancy (Gallagher, 1996). Details of the patients' gynaecological and obstetric history were however not recorded in the clinical dental notes.

Some relatively modern reports inexplicably used obsolete terms; Zhou and co-authors (1989), although citing Waldron and Giansanti (1973) and Waldron (1985) reports, uses the obsolete term 'osteofibroma' to describe one of their 4 FOLs; the 3 others were FD, OF and CF. No reason was given for the use of this term and all cases under its heading were deleted from the report; the report's FDs, and OFs and CFs were included in the appropriate SRs. Exclusion of the 'osteofibroma' cases was made easier because no comment was included with regards to their radiology and thus were readily excluded under 'Criterion 2'.

The differentiation between the COF and FD is very difficult on the basis of the clinical and histopathological features alone. The erroneous view that both lesions are part of the same spectrum still appears to persist in some quarters (Voytek et al., 1995). Differentiation is dependent on the radiographic appearances. Sciubba and Younai (1989) considered that the presence of a well-defined margin was a consistent and reliable radiological marker for COF. A COF in the present report was only considered in 7 of the 16 cases where a differential diagnosis was offered by the receiving surgeon or referring general dental practitioner. It is particularly surprising when the cementoblastoma appeared in the differential diagnosis in three cases. The cementoblastoma is a much rarer lesion of which only 70 cases had been reported in the literature up to 1992 (MacDonald-Jankowski and Wu, 1992) by which time most of the COFs in the present study had been diagnosed. In addition to its rarity, root resorption, an important diagnostic feature of cementoblastoma, was present in only 1 COF in the present study. FD was not offered for any case. The poor performance

for detecting the COF solely on clinical and radiological features has obviously been perceived by others, such as Summerlin and Tomich (1994) and Su and co-authors (1997a and b). They focused on the clinical and radiological features of both COF and FocCOD. This will be taking up again in a later chapter.

Although COF is generally treated by surgical enucleation, resection may be the only option for a lesion which affected nearly the whole hemi-mandible as displayed by Slootweg and Mofty (2005) in their Figures 6.70 and 6.71 in WHO's 'blue book'. Nevertheless, Eversole and co-authors' (1985a and b) reported a 28% recurrence rate following curettage in 22 patients followed up over 38 months. They could not detect any radiological features, which could predict a recurrence. In the absence of a reliable diagnostic or prognostic predictor to indicate the potential of COF for aggressive behaviour or likelihood of recurrence, then long-term follow-up should include radiology. It is obvious that PPDH maintains long term follow-up of its COF patients, but merely providing such a service may not be adequate, many patients can and do discontinue follow-up. Although only one recurred in this study, the fate of the high proportion of the other drop-outs is unknown, unless they return to PPDH with their recurrence.

The differential diagnosis or provisional diagnosis in the present study was wrong in over half of the cases offering one. The only other report to give details of the differential diagnosis was that by Sakota (1977b). This general absence of a differential diagnosis in almost all other reports is surprising, because the differential or provisional diagnosis gives a clearer idea of what the clinician perceives after

examination of the patient and radiographs than from the frequently terse notes in the clinical record. Of course, it is understood that such diagnosis reflects the pattern of disease in that particular community at that particular time, experience and expertise of the clinician, and the classification of lesions then in vogue. Nevertheless, it is interesting that a significant proportion of diagnoses in Sakota's (1977b) report are ameloblastoma as this is likely to reflect the radiolucent and even multilocular presentation of the COFs in that community; this radiological appearance coupled with the fact that most COFs in this Hong Kong community affected the posterior mandible, a site for which ameloblastomas have a predilection (MacDonald-Jankowski et al., 2004c and d). The present study's Mandibular Case 4. offered ameloblastoma as its sole provisional diagnosis. It presented as a multiloculated radiolucency with expansion and tooth displacement. The only major feature associated with ameloblastoma, it lacked, was root resorption (MacDonald-Jankowski et al. 2004c and d)

Other lesions with which COF can be associated include other cemental lesions aneurysmal bone cyst (Dehner et al., 1973) and Paget's disease (Carrillo et al., 1991)

CONCLUSIONS

1. The most recent developing diagnostic dilemma is not whether COF can be differentiated from FD, but rather whether it can be differentiated from CODs, particularly the FocCOD, the most frequently occurring FOL.

2. With the exception of the remarkably significant predisposition for females, the lower proportion of COFs presenting with swelling and with root resorption, the Hong Kong Chinese exhibit clinical and radiological features consistent with those reported in other populations;

3. Female sex hormones may have a role to play in the activation or reactivation of the COF; gynaecological and obstetric histories should be taken in order to understand better the 'life-history' of this lesion.

4. The association of COF subtype with the radiolucent stage could suggest that the COF subtype may indicate the active growth phase of the lesion.

Chapter 7.

FIBROUS DYSPLASIA

INTRODUCTION

The previous SR confined to English language papers on FD included only eight reports amounting to 97 individual cases (MacDonald-Jankowski, 1999). The present SR was considerably more extensive, including reports in major world languages and some lesser-used European languages. It reported also the clinical and radiological manifestations of 21 cases of fibrous dysplasia affecting the jaws of a largely Chinese population and compared these with the 767 cases found in 30 published reports qualifying for inclusion.

AIMS AND RESEARCH QUESTIONS

The primary research question for this SR, or PICO question, is: - "Do other clinical and radiological features improve diagnosis of FD compared with poorly differentiated margins?"

In order to answer this question only those reports, which consider a poorly-defined margin of a histopathologically confirmed FOL as a FD, can be admitted to this SR. In addition to this question there are other supplemental questions, which help to frame the selection criteria for the above PICO question; these are: -

Question 1: What are the clinical and radiological characteristics observed in a Hong Kong community, largely Southern Chinese.

This requires a detailed analysis of the clinical and radiological features observed in a continuous series of cases of FD lesions in a Hong Kong Chinese community admitted to PPDH.

Question 2: Do Chinese/Oriental communities have a different presentation of FD compared with non-Chinese/Oriental communities?

Comparison of the Hong Kong Chinese with the rest of the SR will be addressed in this chapter. Comparison of the Oriental communities with regards to other global communities will be addressed in Chapter 8. To assist the formulation of an answer the SR-included reports will be divided into four global groups, Western, African, Oriental and Latin-American, broadly reflecting ethnic origin.

As the primary aim is to include as many reports as possible a wide search of the literature will be made, including non-English reports. Each report will be scrutinized to determine whether at least some of the features it reports can be included. To this end, reports will not be simply included/excluded, but subject to 'deletion' and 'deduction'. These will be defined in the 'Material and Methods' section.

MATERIALS AND METHODS.

A. Histopathological-based cases derived from a Hong Kong community

The pathology records, between 1982 and 2004, of the PPDH and their clinical notes and radiographs were retrospectively reviewed. In order to diminish the effects of 'expectation bias', which is intrinsic to a retrospective review of cases, the radiographs were read prior to the clinical notes. Each patient's ethnic origin, sex, age, clinical history and findings on examination and the differential or provisional diagnosis were obtained from the clinical records. Each lesion had been radiographed in two planes. Panoramic radiographs were available for all cases and were supplemented by skull views and intra-oral radiographs (periapical and/or occlusal) where appropriate. The generally accepted radiological criteria for FD were established by reference to the literature (including standard texts, such as by White and Pharoah (2004). The radiographs were viewed on a standard illuminated screen under reduced ambient lighting.

The criterion used to determine objectively the degree of definition of the boundary of the lesion was that established by Slootweg and Muller (1990). A lesion was considered to be well-demarcated when its radiodensity changed markedly within a distance of 1 mm when passing from the lesion to the surrounding bone. The effect of the lesion on adjacent structures, such as the teeth, the buccal and lingual cortices, lower border of the mandible and the maxillary antrum, was also recorded. In the SR conducted earlier, the histopathologist was prepared to review any case, which was found to be inconsistent with the radiological findings. The

histopathological findings of the subsequent cases were reported with sufficient detail that there was no doubt that the lesions were histopathologically FOLs.

B. Systematic review

A SR is required to answer the PICO question. A SR requires not only a literature to search, but also selection criteria to sift this literature. As the primary aim is to include as many reports as possible a wide search of the literature will be made, including non-English reports.

Selection Criteria

There were 4 inclusion (Criteria 1 to 4) and 3 exclusion (Criteria A to C) criteria for the SR. Each report will pass through these criteria in strict sequence. Although a report may be excluded by more than one criterion, only the first criterion to exclude a particular report will appear in Table 7.4. [For the sake of brevity only those reports, which cannot be readily included by, reference to their title or abstract will be discussed and cited.]

To identify as many relevant reports and to include as many in the SR; the emphasis is placed on recall rather than precision and on inclusion of as much of each report as the selection criteria would allow. Furthermore, as the aim is to include as many reports or pertinent parts of those reports as possible the use of following terms, exclusion, deletion and deduction, which are normally synonyms,

are specifically defined. 'Exclusion' refers to the 'non-inclusion' of a report to the SR and will be used regardless of whether it is in relation to either 'inclusion' or 'exclusion' selection criteria. Two other terms hitherto not met are 'deletion' and 'deduction'; their use will only be confined to the 'Material and Methods' and 'Results' sections of this FD study. 'Deletion' refers to the removal of those cases within a report which are not consistent with one or more selection criteria and have been reported in sufficient detail to permit their identification and removal from the report, allowing its admission to the SR. 'Deduction' is applied to those reports where 'deletion' is not possible, because the number of non-deletable' cases exceeds 10% of the report. For 'deduction' to be permitted the report must include wholly inclusive words such as 'all' or 'every' qualifying 'patient' or 'case'. 'Almost' appended to 'all', 'every', was later considered to approximate to 100% and considered to be wholly inclusive. Those features to which these words had been applied would have the undeletable cases deducted from the total number of cases for that report and admitted to the SR.

Inclusion Criteria:

Criterion 1. Consistency with the WHO classification.

The study should be consistent with the WHO histological classification of odontogenic tumours (Pindborg et al., 1971; Kramer et al., 1992). Studies particularly those prior to or about the time of the publication of the first edition,

could be included if their definition was consistent with it or if they quoted a publication consistent to it.

Criterion 2. The use of radiographs to determine marginal definition.

Although this is essentially part of 'Criterion 1', because the histopathological and radiological appearances were addressed equally, it is essential that radiological description at least of the periphery be in the reports to be included in the SR. It is assumed that the radiographs would be available to the reporters. It is further assumed that if the radiographs were not available that reference to the clinical notes would provide the required information with regards definition. Although, it is appreciated that reviewers may have different parameters by which they determine marginal definition, some may have not used an objective parameter as that developed by Slootweg and Muller (1990) then reasonable allowance is made to admit reports that may report some FD margins as well-defined. If the report was reported in sufficient detail then it may be possible to identify the non-conforming cases and delete them, thus allowing the rest of the study to pass this criterion. If this were not possible, such studies could only pass this criterion if they did not exceed 10% of the reported lesions as well-defined. Studies which reported that 'almost all', 'the overwhelming majority', would be construed as meaning between 90% to just under 100% of the cases were poorly or ill-defined (that is within the already described 10%) and be thus admitted. On the other hand studies reporting that 'most' or 'majority' of the cases were poorly or ill-defined would not be admitted, because these and similar phrases would be construed to represent 51% to 89% and be thus

well outside the 10% allowance. The strategy for minimising the impact of non-conforming reports on the SR is exclusion, deletion, 'less than 10% rule' and deduction.

Criterion 3. Represent a complete collection of cases of COF

The study should represent a complete collection of consecutive cases of COF, arising within a particular community, occurring in the reporters' caseload. Reports that were merely a selection of cases such as case reports and those studies, which were primarily concerned with specific investigations, or a discrete age group, (such as children) or a particular jaw, were excluded.

Criterion 4. Exclude wholly polyostotic reports.

This criterion reinforces 'Criterion 3'. Reports solely based on the polyostotic form (with or without McCune-Albright syndrome) were excluded, as such reports would be clearly selective. The reason for such a firm policy is that it is generally accepted that the monostotic form predominates in the jaws. Therefore, for such a report to be admitted it would have to expressly declare that cases of the monostotic form would have been admitted if they had been diagnosed. Alternatively, reports including the polyostotic form or McCune-Albright syndromic cases as part of a series of consecutive cases arising within a particular community are admitted.

Exclusion Criteria

Criterion A. Excludes reports already been reported and included in the SR.

It prevents doubling reporting of the same clinical cases, by excluding those reports whose data has already been reported and included in the review. It also excludes reports covering the same clinical material; unless the degree of overlap does not exceed 50% and that there is at least one statistically different feature between them.

Criterion B. Excludes extragnathic cases

The jaws are strictly defined as the whole mandible and the maxillary bone. For inclusion, lesions must all affect the jaws. If they comply with this then consideration of their extent beyond the jaws, to affect the eyes in particular, is permitted.

In order to include only data pertaining to the jaws, it excludes extragnathic cases:

a. Their details could not be identified and deleted.

b. They exceed 10% of the cases.

c. If the 10 % allowance is exceeded then the whole report will be

excluded unless there remains at least one feature that clearly refers only to the jaw lesions. Then the report will be included only with regards to that feature.

Criterion C. Excludes referred cases

It reinforces 'Criterion 3' by minimising dilution of the data arising primarily within a specific community, it excludes those reports which include referred cases, displaying unusual features that may skew the profile of COF within that community, which would in turn skew the SR, if: -

a. Their details could not be identified and excluded, and,

b. They exceed 10% of the cases.

The electronic database interrogation

LILACS and the PubMed interface of Medline were interrogated by the following keyword, "Fibrous dysplasia". The search was limited to humans. This was supplemented by a hand-search of journals listed in Table 3.1. This strategy was further augmented by reference to the bibliographies (or citation lists) of all reports identified by Medline or hand-searching.

Definition of parameters.

The number of years is calculated on the assumption the study begins on the January of the beginning year and ends on the December of the closing year unless stated otherwise in the text.

The 'number of FDs per hospital per year' reflected the number of hospitals contributing to the report and the number of years from which the reported series was derived. Unless it is otherwise clear in the report, the study period at each hospital in a multi-centre report will be assumed to be the same. The advantage of assessing the 'number of FDs per hospital per year' is the ease of comparison of the number of lesions diagnosed as FDs in each hospital (or the average hospital in a multi-centre report) in the course of the average year.

The jaws were further divided into posterior (molar and premolar) and anterior (incisors and canines) sextants. Although the demarcation point between these areas was infrequently expressed, it was taken to occur at a vertical line just distal to the distal surface of the canine.

The lower border of the mandibular alveolus is set by the inferior dental (mandibular) canal and the upper border of the maxillary alveolus on panoramic radiographs is set by the image of the hard palate on panoramic radiographs or lateral cephalographs (MacDonald-Jankowski, 2004a).

Significant differences in frequencies were tested by the X^2 test with $P < 0.05$. Significant differences in age were tested by a Student's t-test with $P < 0.05$.

Handling and analysis of the information acquired from the SR-included reports.

Information in those tables pertaining to each case in the present study was generally entered as a Yes or No or standardised, but on occasion, abbreviated phrases. Information in the SR was generally reduced to numbers. These numbers took account of the number of cases that passed the selection criteria for inclusion, and therefore, may differ from the numbers available in the original report. ING (information not given) was applied whenever information on a particular feature could not be determined (either expressly or impliedly) from the original text.

The present author was prepared to accept that phrases such as "almost all' meant that 90% or above of the cases were referred to, and when such a phrase occurred, the present author would award it a numerical value of 100% of the total number relevant to that particular feature. Furthermore, if this phrase had been applied to features that would include or exclude a report such as the degree of margin definition, or proportion of extragnathic reports, then it would be presumed that the 'number of the non-conforming cases that could not be individually identified and deleted would have lead to exclusion was less than 10%, allowing the report to be included. As excess of 10% with regards to the 2 aforementioned features that were *prima facia* grounds for exclusion that could not be individually

identified and deleted would have lead to exclusion of the report. Nevertheless, provision was made for a report which included over 10% of extragnathic cases which could not be individually identified and deleted, but which contained one or more features which were otherwise accurately quantified then these features would be included and the total number of cases corrected to accord with them. Such scenarios occurred when the phrases containing 'all' or '100% of cases'. These features are likely to be gender, age and presenting symptoms. In those cases for those features for which the report either only offered a non-numerical value such a "most, majority", few", "some" etc, or when the numerical value was compromised by an aforementioned ground for exclusion which could not be individually identified and deleted would have lead to complete exclusion of that report. If it were possible to salvage quantitative data for at least one feature, then that feature would be included in the SR. IIG, ('inadequate information given') would be applied to those features in a partially included report which had been compromised. IIG is also entered against features, which the reporters had not adequately quantified.

RESULTS

A. Histopathological-based cases derived from a Hong Kong community

Twenty-two cases of FD were identified in the records of the department of Oral and Maxillofacial Surgery of the University of Hong Kong for which histopathology reports, radiographs and clinical notes were available. Details of 7

cases detected in the histopathological files in 1992, and the details of the computed tomographic features of 8 cases had already been published, MacDonald-Jankowski (1999) and MacDonald-Jankowski and co-authors (2004b) respectively. The latter contained one case of an Indian male, which had been diagnosed on conventional radiographs outside Hong Kong and had been referred for further investigation and treatment of his maxillary FD, was excluded from the study.

The details of their histopathological presentation, age, clinical presentation or complaint, size and distribution of the remaining 21 FDs in the present study are shown in Table 7.1. Their radiological features and details of their follow-up and recurrence are set out in Tables 7.2 and 7.3 respectively. Twenty were ethnic Chinese and 1 was of Indian origin. (Maxillary Case. 6). One case was bimaxillary (Maxillary Case. 5 and Mandibular Case. 8) and another had Albright's Syndrome. (Mandibular Case. 5); this case also affected malar bone but spared the maxilla.

The age range at presentation was 14 to 44 years; mean 26.71, sd 9.57 years). The mean ages for males and females was 24.0 (sd 8.98) and 28.4 (sd 8.64) respectively; this difference was not significant ($t = 1.14$; 19df; $P > 0.05$). The mean ages for the mandible and maxilla, excluding the bimaxillary case, are 27.08 (sd 9.18) years and 26.25 (sd 11.34) years, respectively; the difference is not significant ($t = 0.17$; 18df; $P > 0.05$).

Table 7.1. Fibrous Dysplasia: Hong Kong Patients; Gender, age, presenting complaint, size and site.

Case No.	Gender & Age(years)	Presenting Complaint	PriorAwareness (years)	Right 8 7 6 5 4 3 2 1	Left 1 2 3 4 5 6 7 8
Maxilla					
1.	M14	Swell.	0.5	Retromolar----------I	
2.	F 16	Ref;AOB	5; inc.> 2 yrs	Retromolar----------I	
3.	M16	Swell. dis	0.01		I---------- Retromolar
4.	M18	Swell;sta.2yr	5		I---------- Retromolar
5.[a]	M26	Swell	FD1st'd @7y.o	Retromolar----------I	
6.[b]	F 33	Swell.	ING	Retromolar----------I	
7.	M33	Swell. dis	13		I---------- I
8.	F 39	Pain, swell	7; inc.>0.1yrs		I----------Retromolar
9.	F41	Swell	1	Retromolar----------I	
Mandible					
1.	M16	Ref;enlarg	1		I----------Condyle
2.	M16	Ref;enlarg	3	Mandibular Foramen ----------I	
3.	F 18	Swell;Pain,N	3; inc.> last 2wk		I----------Condyle
4.	F 21	Swell.	5; inc.> last.yr		I---------- ----------Angle
5.[d]	F 25	Pain	2-3 wks		I----------Condyle
6.	M25	Swelling	0.33	Condyle/Coronoid---------I	
7.	F 26	Ref;swell	10		I----------Mandibular Foramen
8.[a]	M26	teeth;enlarg	FD1st'd @7y.o	Condyle neck----------I	
9[e]	M28	Ref; incid	0	I----------I	
10.	F 30	Ref;l;enlarg	5; surg 5yrs ago	Ramus----------I	
11.	F 35	Incid	0	Ramus----------I	
12.[b,c]	F 41	ING	FD1st'd @10y.o	Condyle----------I	
13.	M44	swell	10	Ramus--------I	

Abbreviations and Notes: AOB, Anterior Open Bite; A.S., Albrights Syndrome; dis, discharge; enlarg. Enlargement; FD1std @14y.o, fibrous Dysplasia first diagnosed at 14 years of age. inc. increase; inc.>, increased greatly; incid, incidental finding; ING, information not given; l, loose teeth; ref, referred; Retromolar, juxtapositioned to pterygoid process; sta,2yr; stable for last 2 years; swell.swelling; teeth, displaced teeth; Yrs, years.

[a] , bimaxillary case; [b] , Indo-Caucasian (South Asian) origin; [c], operated on when 10 and 25 years of age & static since 25 years of age and presents with pathological fracture or non-union; [d], Patient has Albright's Syndrome, has also affected left zygoma (maxillary antrum and alveolus are not affected) and femur; , although histopathology is reported to be principally FD, part appears like a odontogenic myxoma.

Table 7.2. Fibrous Dysplasia: Hong Kong Patients; The radiological features.

Case No.	Predominant radiodensity				Radiological features								
	Radio-lucent	Ground Glass	Peau d'Orange	Sclerosis	Margin Definition	Cortex Absent/ thinned	Expansion	Specific Anatomical Features		Inferior dental canal(IDC) Displaced?	Lamina dura Intact?	Tooth Resorption	Tooth Displacement
Maxilla								Reduction of Maxillary Antral Lumen					
1. M14	No	No	No	Yes	Poor	INA	Yes	Yes		N/A	Yes	No	Yes
2. F16	No	Yes	No	No	Poor	Yes	Yes	Yes		N/A	No	No	No
3. M16	No	Yes[e]	Yes	Yes	Poor	Yes	Yes	Yes		N/A	No	No	Yes
4. M18	No	Yes[e]	No	No	Poor	Yes	Yes	Yes		N/A	INA	Yes	No
5.[a] M26	No	Yes[e]	No	No	Poor	Yes	Yes	Yes		N/A	No	No	Yes
6.[b] F 33	No	Yes[e]	No	No	Poor	Yes	Yes	Yes		N/A	INA	No	No
7. M33	No	Yes[e]	No	No	Poor	Yes	Yes	Yes		N/A	No	No	Yes
8. F 39	No	Yes[e]	Yes	Yes	Poor	Yes	Yes	Yes		N/A	No	No	No
9. F 41	No	Yes	Yes	No	Poor	Yes	Yes	Yes		N/A	Edent.	Edent.	Edent.
Mandible								Inferior border of the mandible Displaced	Thinned				
1. M16	No	Yes	Yes	**No**	Poor	Yes	Yes	Yes	Yes	Yes;d	No	No[d]	Yes
2. M16	No	Yes[e]	Yes	Yes	Poor	Yes	Yes	Yes	Yes	Yes;d	No	No	Yes
3. M18	Yes	Yes	Yes[e]	Yes	Poor	Yes	Yes	Yes	Yes	No	Yes	No	No
4. F 21	No	Yes[e]	No	No	Poor	Yes	Yes	Yes	No	No	No	No	No
5.[d] F 25	No	Yes	Yes	Yes	Poor	Yes	Yes	Yes	Yes	Yes;u	Yes	No	No
6. M25	No	Yes[e]	Yes	Yes	Poor	Yes	Yes	Yes	Yes	Yes;d	No	No[d]	Yes
7. F 26	No	Yes	Yes	Yes	Poor	Yes	Yes	Yes	Yes	Yes;d	No	No	Yes
8.[a] M26	No	Yes	No	Yes	Poor	Yes	Yes	Yes	Yes	Yes;d	No	Yes	Yes
9. M28	No	No	Yes	Yes	Poor	No;thick	Yes	N/A	N/A	N/A	Yes	No	Yes

Case No.	Predominant radiodensity				Radiological features								
	Radio-lucent	Ground Glass	Peau d'Orange	Sclerosis	Margin Definition	Cortex Absent/ thinned	Expansion	Specific Anatomical Features		Inferior dental canal(IDC) Displaced?	Lamina dura Intact?	Tooth Resorption	Tooth Displacement
10. F 30	No	Yes	Yes[e]	Yes	Poor	Yes	Yes	Yes	Yes	Yes:d	No	No	No
11. F 35	No	Yes[e]	Yes	Yes	Poor	Yes	Yes	Yes	Yes	Yes;u	No	No[d]	No
12.[c] F 41	No	Yes[e]	No	Yes	Poor	Yes	Yes	Yes	Yes	No	Edent.	Edent.	Edent.
13. M44	No	No	Yes[e]	No	Poor	Yes	Yes	N/A	N/A	Yes;d	Edent.	Edent.	Edent.

Abbreviations and Notes: d, IDC is displaced downward; INA, Information not available; N/A, not applicable- inappropriate jaw OR affected jaw was edentulous; u, IDC is displaced upward; [a], bimaxillary case; [b], Indian origin; [c], operated on when 10 and 25 years of age & static since 25 years of age and presents with pathological fracture or non-union; [d] , shorter roots; [e], predominant pattern;

Table 7.3. Fibrous Dysplasia: Hong Kong Patients; Follow-up and recurrence

Case No.	Gender & Age(years)	Follow-up?	Review Duration (years)	Discharge by Patient or Surgeon ?	Recurrence? (re-growth after surgery)	Recurrence with similar Histopathology?	Recurrence with similar Radiology?
Maxilla							
1.	M14	Yes	1	Surgeon	No	-	-
2.	F 16	Yes	18	F-U continues	No	-	-
3.	M16 29	Default(1982) Yes(from'95)	0(1'82) 11('95)	Patient (1982) F-U continues	Yes	No biopsy	Becoming more radiodense
4.	M18	Yes	1.5	Patient	No	-	-
5.[a]	M26	Yes	18	F-U continues	No	-	-
6.[b]	F 33	Yes	10	Patient	No	-	-
7.	M33	ING					
8.	F 39	Yes	8	F-U continues	No	-	-
9.	F41	Yes	24	F-U continues	Yes		
Mandible							
1.	M16	Yes	10	F-U continues	No	-	-
2.	M16	Yes	17	F-U continues	No	-	-
3.	F 18	ING					
4.[d]	F 21	Yes	0.86	Patient	No	-	-
5.[e]	F 25	Yes	2	F-U continues	No	-	-
6.	M25	Yes	13	Surgeon	No	-	-
7.	F 26	Yes	7	Patient	No	-	-
8.[a]	M26	Yes	18	F-U continues	No	-	-
9.	M28	Yes	6	Patient	No	-	-
10.	F 30	Yes	11	F-U continues	Yes ('95)	unremarkable	No earlier films
11.	F 35	ING					
12.[b,c]	F 41	Yes	1	Patient	No	-	-

Case No.	Gender & Age(years)	Follow-up?	Review Duration (years)	Discharge by Patient or Surgeon ?	Recurrence? (re-growth after surgery)	Recurrence with similar Histopathology?	Recurrence with similar Radiology?
13.	M44	ING					

Abbreviations and Notes: ING, information not given; l, loose teeth; ref, referred; Retromolar, juxtapositioned to pterygoid process; swell.swelling; teeth, displaced teeth. Yrs, years.[a] , bimaxillary case; [b,] Indo-Caucasian (South Asian) origin; [c], operated on when 10 and 25 years of age & static since 25 years of age and presents with pathological fracture or non-union; [d], Patient has Albright's Syndrome, has also affected left zygoma (maxillary antrum and alveolus are not affected) and femur.

Although this mean age at first presentation at PPDH was higher than that of the SR, when prior awareness of the lesion is taken into account, then the mean age is 20.5 years (sd 9.41; (n = 20, because the non-contributory Maxillary Case 6 was excluded)). Following exclusion of the bimaxillary case, the mean ages for the 12 mandible was 21.42 (sd 8.35) and the 7 maxilla was 21.28 (sd 10.56); t = 0.00; 17df; $P > 0.05$.

The main modes of presentation is swelling or enlargement in 17 jaws presented at 25.24 (sd 8.51), or in 16 cases (including the bimaxillary case) at 25.19 (sd 8.79). Five of the 7 referred patients had been specifically referred by their general dental practitioner for investigation of the symptoms and signs associated with the FD. Only 2 lesions were observed as incidental findings. The FD in 1 referred patient was observed as an incidental finding upon admission to PPDH (Maxillary Case 2). The remaining patient was referred for an anterior open bite. Four of the 20 patients, who were aware of their lesions for a number of years, reported an increase in size prior to their presentation; all 4 were female.

The 18 cases in the present study accompanied by swelling or enlargement reflected SR's 72% ($X^2 = 2.04$; 1df; $P > 0.05$). The 3 cases associated with pain occurred in older patients (27.3 sd 10.7 years) in comparison with the 18 cases which did not report pain (25.0 sd 8.31); this was not significant (t = 0.34; 18df; $P > 0.05$). This low occurrence of pain and the discovery of FDs as incidental findings in 2 cases were just as frequent as that observed for the rest of the SR ($X^2 = 0.97$ and 0.29 respectively; 1df; $P > 0.05$).

Eight of the 9 lesions affecting the maxilla extended throughout the whole hemi-maxilla; only one case affected the posterior maxilla alone (Maxillary Case 7). The association between the hemi-maxilla and hemi-maxillary involvement is highly significant; $X^2 = 18.34$; 1df; $P < 0.001$ (the bimaxillary case was excluded). Four other mandibular cases occupied the hemi-mandible backwards to the mandibular foramen. The mandibular lesion of the bimaxillary case not only affected the whole hemi-mandible, but also crossed the midline to involve extensively the contra-lateral side. Another case affected the anterior half of the body bilaterally (Mandibular Case 8). Six other mandibular cases affected the posterior sextants only.

FDs in the present report (Table 7.2) and SR (Table 7.7) appeared radiographically as poorly-defined structures of radiopacity varying from ground-glass and peau d'orange to sclerotic (Table 7.7). The differences between their proportions were not significant ($X^2 = 0.8$, 2.37 and 0.9 respectively; 1df; $P > 0.05$).

The differential or, more appropriately, the provisional diagnosis was provided in all cases by the referring hospital clinicians and consisted only of FD.

Follow-up and recurrence was detailed on Table 7.3. Seventeen patients were followed-up. No information was available on the remaining 4. Six patients discontinued follow-up after a mean of 4.4 years (sd 3.82); the surgeon discharged 2 patients, after 1 and 13 years follow-up. One patient (Maxillary Case 3) defaulted

initially, but returned to follow-up after a recurrence. Only one other recurred (Mandibular Case 10.).

B: Systematic review

Selection Criteria.

Many of the reports were automatically rejected because they were single case reports or review articles. Those excluded under specific exclusion criteria are set out in Table 7.4.

Table 7.4. Fibrous Dysplasia: Excluded reports

Selection Criterion	Report (1st author's surname and date of publication)	Gp.	Language of Publication
1	Wu et al. (2005)	O	Chinese
3	Pontual et al. (2004)	L	English
2	Bencini et al. (2003)	L	Spanish
1	Olavarria et al. (2003)	L	Spanish
1	Akintoye (2003)	W	English
2	Sobral et al. (2003)	L	Portuguese
2	Becelli et al. (2002)	W	English
1	Pollandt et al. (2002)	W	German
B	Ozek et al. (2002)	W	English
A	Ogunsalu et al. (2001)	A	English
2	Kuyama et al. (2000)	O	English
A	MacDonald-Jankowski (1999)	O	English
B	Yeow & Chen (1999)	O	English
2	Barcelos et al. (1998)	L	Portuguese
1	Cardona et al. (1998)	W	English.
1	Iannetti et al. (1984)	W	Italian
3	Petrikowski et al. (1995)	W	English
1	Camilleri (1991)	W	English
2	Barbosa et al. (1991)	L	Portuguese
1	Perrin et al. (1991)	W	French
2	Blanchard et al. (1990)	W	French

Selection Criterion	Report (1st author's surname and date of publication)	Gp.	Language of Publication
1	Kransdorf et al. (1990)	W	English
1	Villalobos Aracena (1990)	L	Spanish
1	Chen & Nordhoff (1989)	O	English
2	Nakade et al. (1989)	O	Japanese
2	Weerapradist et al. (1989)	O	English
1	Chomette et al. (1987)	W	French
1	Jammet et al. (1987)	W	French
2	Bukal et al. (1986)	W	German
1	Gundach (1986)	W	German
1	Vergara-Piedra et al. (1986)	A	Spanish
1	Buchmann&Bienengraber (1986)	W	German
1	CabaleiroPelayo (1985)	L	Spanish
1	Palomba &Alfieri (1985)	W	Italian
1	Canigiani&Wickenhauser (1982)	W	German
1	Sherman et al. (1982)	W	English
1	Naddachina&Gudaidulina (1980)	W	Russian
B	Boysen et al. (1979)	W	English
1	Chassagne et al. (1979)	W	French
2	Deeb et al. (1979)	W	English
1	Stypulkowska et al. (1979)	W	French
1	Obisesan et al. (1977)	A	English
2	Daramola et al. (1976)	A	English
3	Smoler Berkovsky (1975)	L	Spanish
3	Rohlin & Nosslin (1974)	W	English
2	Williams et al. (1974)	A	English
1	Williams & Faccini (1973)	A	English
1	Biedermann et al. (1972)	W	German
1	Bonne (1972)	W	German
2	Gibson & Middlemiss (1971)	W	English
1	Hattowska et al. (1970)	W	Polish
1	Reynaud & Courson (1970)	W	French
1	Chung et al. (1969)	O	English
1	Contreras et al. (1969)	W	Spanish
2	Dahlgren et al. (1969)	W	English
2	Henry (1969)	W	English
1	Odeku et al. (1969)	A	English
2	ColmeneroRuiz&Carretero(1968)	W	Spanish
1	Anand et al. (1967)	A	English
2	Hadders (1967)	W	Dutch
1	MacKenzie (1967)	W	English
1	Houston (1965)	W	English
1	Milanesi & Molinari (1966)	W	English
1	Pound et al. (1965)	W	English

Abbreviations: A, African; L, Latin-American; O, Oriental; W, Western.

There was no significant difference between the proportions of English with non-English SR-excluded reports (Table 7.4.) with the SR-included reports (7.5.) for the 4 global groups; $X^2 = 4.42$; 3df; $P > 0.05$.

Criterion 1.

Thirty-nine reports were excluded under 'Criterion 1.' General or medical pathological rather than oral and maxillofacial pathological sources were likely to be rejected unless they expressed a clear understanding that although the FD and COF have the similar FOL histopathology, they can be distinguished by radiology; the former has a poorly-defined margin, whereas the latter has a well-defined margin. Unfortunately, most medical reports are more likely to view many if not all COFs as variants of FD. This is reflected in their basic authorities on FOLs, they used Schajowicz' (1993) WHO classification of bone tumours, Vojtek and co-authors (1995), and Dorfman and Czernick (1998) rather than either edition of the WHO's odontogenic classification or other central authorities already cited. Therefore most fail both 'Criterion 1' and 'Criterion 2' and are thus excluded, because they must included an unquantifiable number of COFs. Among such recent reports are to be found not only head and neck surgeons such as Yeow and Chen (1999), and Wu and co-authors (2005), other medical specialists, Villalobos Aracena (1990) and Katz and Nerad (1998), but also oral and maxillofacial authorities, such as Becelli and co-authors (2002), Cardona and co-authors (1998). Vergara Piedra and co-authors

(1986) did not quote the above authors and treated most of their lesions by enucleation, which by implication suggested that many of them must have been COFs. Barbosa and co-authors (1991) and Sobral and co-authors (2003) based their reports solely on histopathology. Although 2 other Latin-American dental reports (Rados, 1986 and Bordagaray and Bordagaray, 1996) did not refer to either edition of the WHO classification or other primary sources it was clear that they both referred to FDs, both with regards to histopathology and radiology. On the other hand Bencini and co-authors (2003) reported the histopathology broadly consistent with the WHO's classification, and although they declared that the FD's margins are very poorly-defined, they later declared that it was not possible to differentiate between COF and FD radiologically. As this implied the presence of COFs among their 6 cases of FDs, their report was excluded. Other excluded reports are those, albeit of a former era, Dahlgren and co-authors (1969), Chung and co-authors (1969), Pound and co-authors (1965), Reynaud and Courson (1970) and Cangiano (1971). Almost all of these studies considered FD and COF to be synonymous; 3 of Cangiano's 5 cases of FDs were clearly not only COFs but also CODs.

The reports on FDs by Obwegeser and co-authors (1973), Talbot and co-authors (1974), Bordagaray and Bordagaray (1997), and Garau and co-authors (1997) clearly included COFs, but were able to report them in sufficient detail to allow the COFs to be identified and removed. For the reason already discussed these deleted COFs could not be included in the COF SR. On the other hand it was possible to transfer a clear case of FD from Adekeye and co-authors' (1990) COFs, because they concurrently reported FDs.

Criterion 2.

Eighteen reports were excluded under 'Criterion 2.' Ozek and co-authors (2002) were clearly aware of COFs, but merely stated that only 'most' lesions (FDs) were poorly-defined; this statement was inadequate for inclusion. This report would also have been excluded under 'Criterion B' because over 10% of its cases were extragnathic which could not be individually identified and deleted. Karja and Rasanen (1972) used the very imprecise 'diffuse shadowing' which could apply within its context either to a poorly-defined margin and a 'ground glass' appearance. This report was salvaged from exclusion by the reference to their COFs' well-defined margins, and the reasonable inference that the FDs were poorly-defined.

Obisesan et al. reported 9 out of their 25 FD cases as well-defined; these were identified and deducted, allowing the reminder to enter the SR.

Criterion 3.

Four reports were excluded under 'Criterion 3.' The reports by Pontual and co-authors (2004), reported an indeterminate number of patients from other parts of Brazil outside their state. Petrikowski and co-authors' (1995) report was clearly based on a selection of cases. Smoler-Berkovsky and co-authors' (1975) report was confined to children and adolescents. Jones and co-authors (2006a) also reported children but as it could be combined with another report on adults in the same

community for the same period (2006b) they were both combined and included as one report.

Ogunsalu and co-authors (1998) included 2 cases which had already recurred; they were identifiable, were excluded and the rest allowed to enter the SR. Cases which recurred were not excludable *per se*, provided they provided information about the primary presentation, particularly year of onset and presentation.

Criterion 4

No reports were excluded under this criterion, because although Akintoye and co-authors' (2004) report was purely syndromic, it had been readily excluded on its title at the literature assembly stage, prior to application of selection criteria. Their 2003 report (Akintoye et al., 2003), which included non-syndromic cases within what appeared to be a consecutive case series, had already been excluded under 'Criterion 2' because they used solely histopathological features to determine the diagnosis of FD.

Criterion A.

Three reports had been excluded under 'Criterion A'. The report by MacDonald-Jankowski (1999a) is contained within the present study and SR and is excluded. Yamamoto (1985) reported the same material as Sakato (1977b), but added more detail and was therefore included under Sakato (1977b). Ogunsalu and co-

authors reported the same FD material three times (Ogunsalu et al., 1998; Ogunsalu et al., 2001 and Ogunsalu, 2003), the first report (Ogunsalu et al., 1998), the more detailed, was alone included. Only the latest excluded Ogunsalu report (Ogunsalu et al., 2001) was included in Table 7.4.

Criterion B.

Four extragnathic reports were excluded under this criterion. All 4 of Slootweg and Muller's (1990) polyostotic cases appeared to be extragnathic but as they were very readily identified as a group they were all deleted *en bloc*, leaving the monostotic cases to enter the SR. The reports by Talbot and co-authors (1974), Adekeye and co-authors (1980), Garau and co-authors (1997) and Yetiser and co-authors (2006) reported their extragnathic cases with sufficient detail for their deletion allowing the remaining cases to be included in the SR. The extragnathic cases of Gosserez and co-authors (1968), Ajagbe and co-authors (1983), Kowalik and co-authors (1996), Pinsolle and co-authors (1998) and Matzuzaka and co-authors (2002), could not be individually identified and could not therefore, be deleted. Those cases in the reports by Ajagbe and co-authors (1983) and Matzuzaka and co-authors (2002) did not exceed 10% (7% of 98 and 5% of 56 cases respectively) and were wholly included in the SR.

Deduction was applied in three reports in which the proportion of extragathic cases exceed 10%. Gosserez and co-authors' (1968) extragnathic cases (43% of 14 cases) were identifiable and 'deducted', salvaging the gnathic part, allowing only

number of maxillary and mandibular cases to enter the SR. Deduction of the extragnathic cases (30% of 30) in the report by Kowalik and co-authors (1996) salvaging only the gender, whereas in the report by Pinsolle and co-authors (1998) (26% of 29 cases were extragnathic); almost all features survived 'deduction' and entered the SR, except the 'number of FD cases per hospital per year' and site.

Criterion C.

No reports were excluded by this criterion. Waldron and Giansanti's (1973) report was salvaged because the cases referred from outside the community were readily identifiable and were excluded, allow the rest to enter the SR.

The present study and the SR

Thirty-one reports of series of cases were included in the SR, including the present study. These 31 reports include 2 sets of combined reports (Sakato, 1977b and Yamamato, 1985; Jones and Franklin, 2006a and b) as if they were just 2 (Sakato, 1977 and Jones and Franklin, 2006) of the 31. There is no statistical difference for the proportion of English-language published reports for the 30 SR-included (Note: the present study although is SR-included is excluded from this comparison) in Table 7.5. or the 67 excluded (Table 7.4); $X^2 = 1.44$; 1df; $P > 0.05$. The distribution of the clinical, decade at first presentation and radiological details extracted from each of the SR-included reports were summarised in Tables 7.5, 7.6

and 7.7 respectively. A statistical analysis of the 30 already-published reports is compared to the present study in Table 7.8.

There were 15 'Western' (including 1 each from India and Turkey), 5 African (including 1 from Jamaica), 9 Oriental and 2 Latin-American reports (see Map 4.). A classic representative of FD is displayed in Figure 3. The most unusual feature is the shape of the roots of adjacent molars. They appear to exhibit resorption, but this may merely represent exceptionally abnormal root development within dysplastic bone.

Furthermore, non-Whites, particularly Black patients, were well represented in most 'Western' reports, especially that by Waldron and Giansanti. (1973)

The 'number of FDs per hospital per year' was calculated whenever possible for each report and displayed in Table 7.5. The 'number of FDs per hospital per year' was not determinable for 8 reports. The 'number of FDs per hospital per year' fell from 2.1 (sd 2.40) up to 1990, to 1.6 (sd 1.00) FDs per year from and including 1990; this difference was not significant ($t = 1.0$; 18df:$P > 0.05$).

Most reports included the patients' sex, age and site affected, but only 12 included any presenting clinical details (Table 7.5). Ten reports considered whether their cases did or did not recur after treatment; 6 were published since 1990. The SR's recurrence rate was 8%; the difference between the HK report and the SR was insignificant (Table 7.8)

Table 7.5. Fibrous Dysplasia: Systematic review; Analysis of the included reports.

First Author (year)	National and/or Ethnic origin (Number of Hospitals(H) and number of Cities(C))	Period covered	No of FDs (No. per hospital per yr)	Polyostotic (Al. Syn)	Craniofacial	Gender	Age mean(range) in years *Pre-presenting duration mean (range) in years*	Presenting Signs and Symptoms			SITE		Comments
						Male Female		Swelling	Pain	Other	Mandible Ant. Post.	Maxilla Ant. Post.	Follow-up (FU) and Recurrence
Gosserez (1968)	French (1H:1C)	ING	6* *Orig 14*	ING	IIG*	ING	ING *ING*	ING	ING	ING	3	3*	*Deleted 11 EGs FU ING
Schmaman (1970)	Sth African (1H:1C)	13 years	5 (0.4)	ING	1	ING*	ING *ING*	ING	ING	ING	4	1	At least 1 F FU ING
Karja (1972)	Finnish (1H:1C)	1964-1970 6 years	5 (0.8)	ING	ING	3 2	**20** (6-56) *ING*	ING	ING	ING	2	3	 FU 2-6 yrs 0 recur
Eversole (1972)	US (9W:3B) (1H:1C)	ING	12	0	2	7 5	**27**(ING) *ING*	ING	ING	ING	0 9	1 5	 FU ING
Obwegeser (1973)	Swiss (1H:1C)	1963-1973 10 year	5 (0.5)	0	0	1 4	**24**(7-55) *7.4(0-25 (childhood))*	5	0	1Incid.	2	3	Excluded 1 pol & 1 JOF & 2Che FU 2 yrs 0 recur
Waldron (1973)	US (10W:6B) (1H:1C)	1957-1971 14 years	16 (1.1)	ING	2	7 9	**26**(5-54) *IIG(upto30+)*	16	0	0 Incid.	6	10	 FU ING
Kawai (1974)	Japanese (1H:1C)	20 years	12(0.6)	ING	ING	ING	ING *ING*	ING	ING	ING	ING	ING	 FU ING
Talbot (1974)	UK (1W:2B) (1H:1C)	1959-1972 24 years	3 (0.1)	0	0	1 2	**20**(13-26) *ING*	3	2	0 Incid.	1	2	2 COF excluded FU ING

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	No. per hospital per yr]	Polyostotic (Al. Syn)	Craniofacial	Gender Male Female	Age	Swelling	Pain	Other	Mandible Ant. Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Langdon (1976)	UK (1H:1C)	1966-1975 10 years	15 (1.5)	0	ING	ING	**24**(ING) *IIG*	ING	ING	ING	3	12	 FU ING
Sakato(1977)	Japanese (1H:1C)	ING	49	ING	0	24 25	**30**(7-17)* *ING*	47	4	1 NO 0 Incid.	12*	37*	* modified by Yamamato FU ING
Adekeye (1980)	Nigerian (1H:1C)	1 year	5 (0.5)	0	3	3 2	**19**(14-27) *6.3(0.33-13)*	4	0	2tthdispl 1Atr.eye 0 Incid.	0 1	4	7 COFs FU 2 recur
Ajagbe (1983)	Nigerian (1H:1C)	1966-1980 15 years	98 (6.5)	0	1	42 56	**24** *(11-62)*[x] *ING (0.3-4.0)*	IIG	IIG	IIG	35*	56*	*7 (7%)EGs deleted 13 FU 5yrs 11 recur
Rados (1986)	Chilean (1H:1C)	ING	6	ING	ING	5 1	**14** (5-19) *IIG*	ING	ING	ING	0	6 0 6	 FU ING
Nicopoulou (1988)	Greek (1H:1C)	ING	4	ING	1*	1 3	**23** (11-42) *4(2-7)*	4	0	0 Incid.	2*	3*	* 1 case is bimaxillary FU ING
Ye (1989)	Chinese (1H:1C)	ING	43	8	18	22 21	**22** (ING) *ING*	ING	ING	ING	IIG	IIG	 FU 1-15 years
Yoon (1989)	Korean (1H:1C)	1977-1986 10 years	31 (0.5)	ING	ING	12 19	ING (10>-<69) *IIG(0.02-20)*	27	19	1 Incid 1 NO	3 0	4 20	4 jaws are not given FU ING
Zhang (1989)	Chinese (1H:1C)	ING	16	2	ING	IIG	IIG *ING*	ING	ING	ING	3	11	2 poly - EGs FU ING
Zhou (1989)	Chinese (1H:1C)	1966-1985 20 years	79 (4.0)	8	ING	ING	IIG *ING*	ING	ING	ING	IIG	IIG	 FU ING

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	No. per hospital per yr]	Polyostotic (Al. Syn)	Craniofacial	Gender Male Female	Age	Swelling	Pain	Other	Mandible Ant. Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Slootweg (1990)	Dutch (1H:1C)	ING	7 *monoost*	0	0	3 4	**31**(ING)	ING	ING	ING	5	2	Deleted all 4 polyost-EG
							ING						FU ING
Swaroop (1990)	Indian (1H:1C)	1963-1981 18 years	1 (0.1)	ING	ING	ING	ING	ING	ING	ING	0	1	
							IIG(0.1-6)						FU ING
Lu (1993)	Chinese (1H:1C)	1957-1990 33 years	117 (3.5)	15	9	65 52	**14**(3-39)	ING	ING	ING	49	66	2 jaws not given
							ING						FU ING
Kowalik (1996)	Polish (1H:1C)	1970-1995 16 years	21* (1.3) *Orig. 30*	0	2	IIG*	ING(IIG)	21 *assym*	0	0 Incid.	8*	15*	*9(30%) EGs delete&deduced 2 cases both jaws Resected almost all
							ING						FU 0 recur
Bordagaray (1997)	Chilean (1H:1C)	1977-1996 10 years	2 (0.2)	ING	ING	2 0	**19**(10-28)	2	1	1 NO 2 pus 0 incid	0	2	28/10yrs 3/9 ops respective
							4.5 (0.5-6)						
Garau (1997)	Italian (1H:1C)	1984-1995 11 years	7 (0.6)	0	2	2 5	**34**(9-72)	IIG	IIG	IIG majIncid	1 (5) 1 1 Xmidline	1 1	1 EG FD deleted & 4COFs exclude
							ING						3 recur FD/COF

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	No. per hospital per yr]	Polyostotic (Al. Syn)	Craniofacial	Gender Male Female	Age	Swelling	Pain	Other	Mandible Ant. Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Ogunsalu (1998)	Jamaican (1H:1C)	1980-1995 15 years	15(1.1)	0	IIG	5 10	**26**(10-47)	15	1	1ulcer 0 incid	0 5	4 (10) 3	
							ING		Same case				1 recur
Pinsolle (1998)	French (1H:1C)	1980-1995 15 years	20*(1.3) *Orig.29*	IIG*	IIG*	IIG*	IIG*	IIG*	IIG*	IIG*	19	1*	* 5(17.2%) EGs deleted
													Mean FU for 8 yrs.
Matzuzaka (2002)	Japanese (1H:1C)	1966-2001 35 years	56* (1.6)	IIG*	ING	21 35	**28**(<0->79)	ING	ING	ING	49*	38*	*Majority must be polyost 3(5.4%) EGs
							ING						FU ING
Simon (2002)	Tanzanian (national)	1982-1997 15 years	46 (3.1)	ING	ING	ING	ING	ING	ING	ING	ING	ING	Added 28 OFs & 2 CF
							ING						FU ING
Jones (2006)	UK (1H:1C)	1973-2002 30 years	55* (1.8)	ING	ING	27* 28*	**27***(ING)	ING	ING	ING	ING	ING	*combines 2 reports
							ING						FU ING
Yetiser (2006)	Turkish (1H*:1C)	1990-2004 14 years	10* (0.7) *Orig. 26*	0	9	10 0	**20**(18-22)	9	5	1 loss of vision 0 incid	0 1 condyle	9	* 14 EGs deleted
							ING						12 FU 0 recur
Present (2006)	Hong Kong (1H:1C)	1982-2004 22 years	21 (1.0)	1A	1	10 11	**27**(10-44)	18	2	2 Incid 1 Numb	0(13*#) 7	0(9*@) 8	* 1 bimax # 2 cross mid
							0.7 (0-10)						FU 2 recur

First Author (year)	(Number of Hospitals(H) and number of Cities(C))	Period covered	No. per hospital per yr|	Polyostotic (Al. Syn)	Craniofacial	Gender Male Female	Age	Swelling	Pain	Other	Mandible Ant. Post.	Maxilla Ant. Post.	Comments (FU) and Recurrence
Total number of cases			788	34[b]	51[c]	273[d] 294[d]	**24**[e](5-79) *2.7*[f]*(0-20)*	167	34	4 Incid[i] 3Ocul[j]	240 4[l] 24[l]	336 10[l] 37[l]	19[m] recur
Percent of cases				6	13	48 52		72	17	7 Incid[i] 15 Ocul[j]	41[k] 14[l] 86[l]	59[k] 21[l] 79[l]	8 recur
Total number Of series			(23)[a]	16	16	21	21(14) *5 (9)*	12	12	12 Incid[i] 2 Ocul[j]	26[k] and 8[l]		10
Percent of 31 series			(74)	39	35	68	68(45) *16(29)*	39	39	39 Incid 8 Ocul	84[k] and 26[l]		32

Abbreviations and Notes: Al. Syn., Albrights syndrome; asymp, symptomless & incidental finding; Atr.eye, atrophic eye; bimax, bimaxilllary; CF, craniofacial; Che, Cherubism; EGs, extra-gnathic cases; epipho, epiphora; exclu, excluded; incid,incidental finding; JOF. Juvenile Ossifying Fibroma; majincid., majority were incidental findings; mand, mandible; mid, midline; NO, nasal obstruction; Ocul, includes any visual abnormality from proptosis to loss of vision; pol., polyostotic; propt, proptosis; rec, recurrent; refs, referred cases; Sth, South.

Key	Number of reports	Total number of cases
a. No.FD/H/Yr	23	623
b. Polyostotic	12	508
c. Craniofacial	13	400
d. Gender	22	567
e Mean Age	21	660
f. Awareness	5	37
g. Swelling	12	182
h. Pain	12	182
i Incidental	12	182
j. Ocular	2	20
k Site: Jaw	26	576
l. Site:Ant./Post	6	Md: 100; Mx:100
m. Follow-up/ Recurrence	8	252

Table 7.6. Fibrous Dysplasia: Systematic review; Distribution of cases according to age (in decades). *The number of males and females are in parentheses*

Decade	Obwegeser	Waldron	Talbot	Adekeye	Ajagbe	Rados	Yoon	Garau	Ogunsalo	Matsuzaka[b]	Yetiser[c]	CONTINUED
0-9	3 (1:2)	1 (0:1)	0	0	11	1(1:0)	0	1(1:0)	0	2(0:2)	0	
10-19	1 (0:1)	6 (3:3)	1 (1:0)	4(2:2)	44	5(4:1)	12	1(1:0)	4(2:2)	13(8:5)	1(1:0)	
20-29	0	3 (3:0)	2 (0:2)	1(0;1)	23	0	12	2(0:2)	7(3:4)	17(8:9)	9(9:0)	
30-39	1 (1:0)	3 (0:3)	0	0	13	0	3	1(0:1)	2(1:1)	14(2:12)	0	
40-49	0	2 (1:1)	0	0	5	0	2	0	2(0:2)	6(3:3)	0	
50-59	1 (0:1)	1 (0:1)	0	0	1	0	0	0	0	1(0:1)	0	
60-69	0	0	0	0	1	0	2	1(0:1)	0	2(0:2)	0	
70-79	0	0	0	0	0	0	0	1(0:1)	0	0	0	
80-89	0	0	0	0	0	0	0	0	0	0	0	
Total	6 (2:4)	16 (7:9)	3 (1:2)	5(2:3)	98	6(5:1)	31	7(2:5)	15(6:9)	5(21:34)	10(10:0)	

Abbreviations and Notes: [a], 11-20 etc; [b]1 female's age is unknown; [c] only 6 females out of 26 craniofacial cases

Table 7.6. (Continued). Fibrous Dysplasia: Distribution of cases according to age (in decades).
The number of males and females are in parentheses

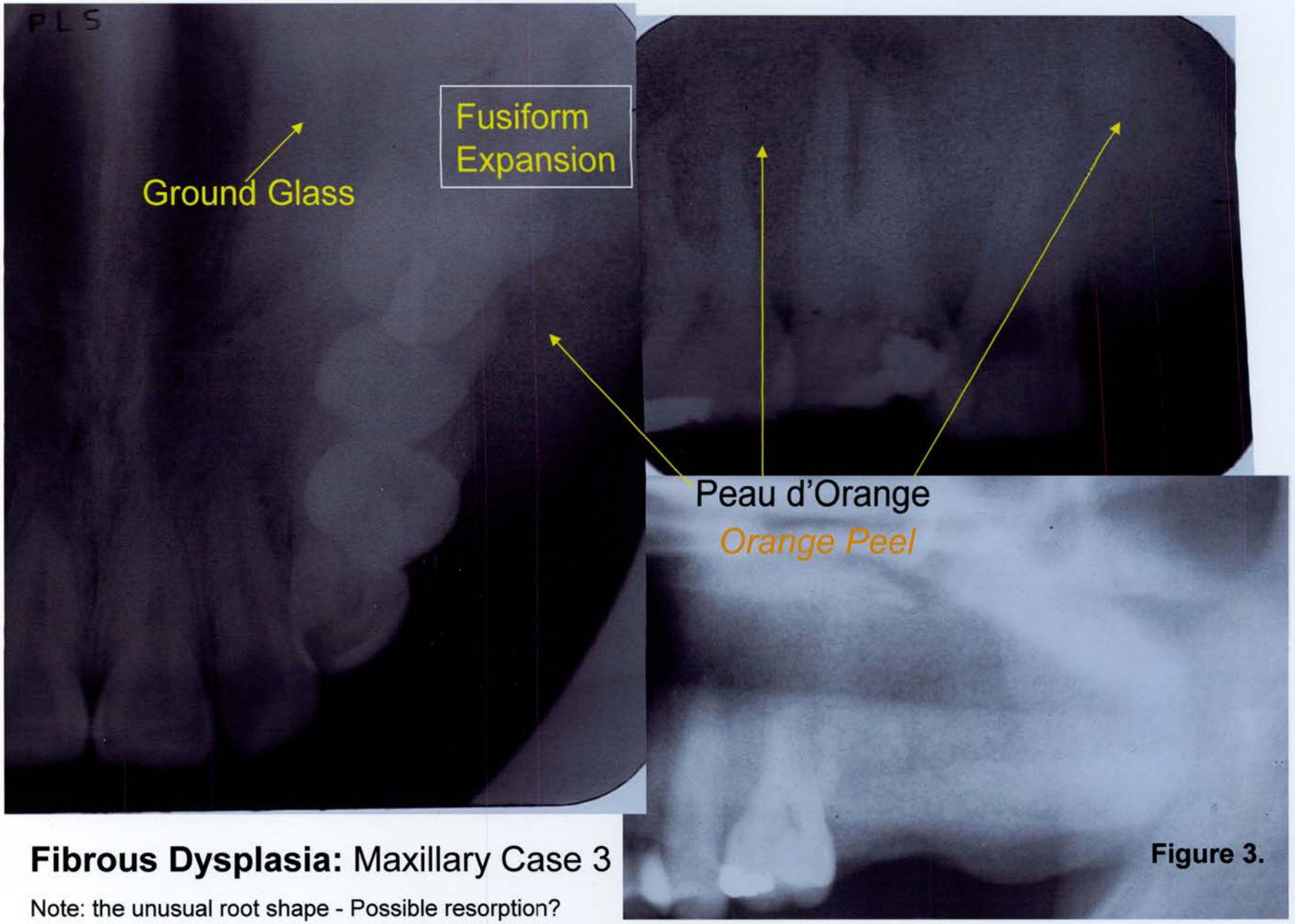
Decade	Total	Present Study	Overall Total	Decade in % of Total	Percentage of Males/Decade
0-9	19(3:5)	0	19(3:5)	7	38
10-19	92(22:14)	7(5:2)	99(27:16)	36	63
20-29	76(23:18)	6(3:3)	82(26:21)	30	55
30-39	37(4:17)	5(1:4)	42(5:21)	16	19
40-49	17(4:6)	3(1:2)	20(5:8)	7	38
50-59	4(0:3)	0	4(0:3)	1	0
60-69	6(0:3)	0	6(0:3)	2	0
70-79	1(0:1)	0	1(0:1)	1	0
80-89	0	0	0	0	0
Total	252(56:67)	21(10:11)	273(66;78)	99	44

Abbreviations and Notes: [a], 11-20 etc; [b]1 female's age is unknown;
[c] only 6 females out of 26 craniofacial cases

Table 7.7. Fibrous Dysplasia: Systematic review; Analysis of the radiology in the included reports.

Radiological Features / Author (year)	No of cases	Predominant Radiographic Presentation					Shape of mandibular lesions		Expansion						Tooth Displace-Ment		Root Resorpt-Ion	
		Radio-lucent	Radiopaque Ground Glass	Peau d'Orange	Sclerotic	Other	Fusi-form	Multi-locular	Bucco-Lingual		Lower Border of the Mandible displaced (and/or eroded)		Antral Involvement					
									Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Schmaman (1970)	5	0	5	0	0	0	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING
Eversole (1972)	15*	3	6	0	0	6m	ING	3	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING
Waldron (1973)	22	0	16[a]		0	4s	IIG	ING	22	0	10	0	22	0	9	13	0	22
Adekeye (1980)	5	0	1	0	4	1	ING	ING	4	0	1	0	4	0	3	1	ING	ING
Zhang (1989)	16	1	12	0	2	1op	16	0	ING	ING	ING	IIG	IIG	ING	0	16	0	16
Swaroop (1989)	1	0	ING	ING	ING	1op	ING	ING	1	0	N/A	N/A	1	0	ING	ING	ING	ING
Lu (1993)	117[b]	6[b] cy	39[b]	ING	6[b]	37[b] mi	49	ING	117	0	ING	ING	ING	ING	IIG	IIG	0	75
Garau(1997)	7	0	6[a]		1	1p	ING	ING	ING	ING	ING	ING	ING	0	IIG	IIG	ING	ING
Ogunsalu(1998)	15	2	2	3	0	6op	ING	ING	15	0	ING	ING	3	1	ING	ING	ING	ING
Yoon	31	1	13	0	3	2m	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING	ING
Present	22*	0	13	3	1	5v	13	0	22	0	11	0	9	0	10	10	2	18
Summary	256*	13/256	91/226	6/109	17/255	64/256	76/155	3/53	181	0	22	0	39	1	22	40	2	131
		5%	41%	6%	7%	25%	50%	6%	100%		100%		98%		35%		2%	
		Percent of 253[b] less ING & combined groups																

Abbreviations and Notes: *, denotes number of jaws in stead of patients; [a], 16 cases which displayed either ground glass OR peau d'orange; [b], out of 75 cases for which there were a 'complete' set of radiographs; for all cases the radiographs would appear to have been adequate for other more general features including the determinantion of the poorly-defined margin; C, cotton-wool; cy, cyst-like; IIG, Inadequate information given; IIG*, If displacement occurred it was not marked; ING, Information not given; m, mottled; mi, mixed; Multiloc., multilocular; N/A, Not applicable; op, opacification of antrum or to varying degrees; p. pagetoid; w, whorled; v, varied, varying proportions of the preceding presentations with not one predominating.

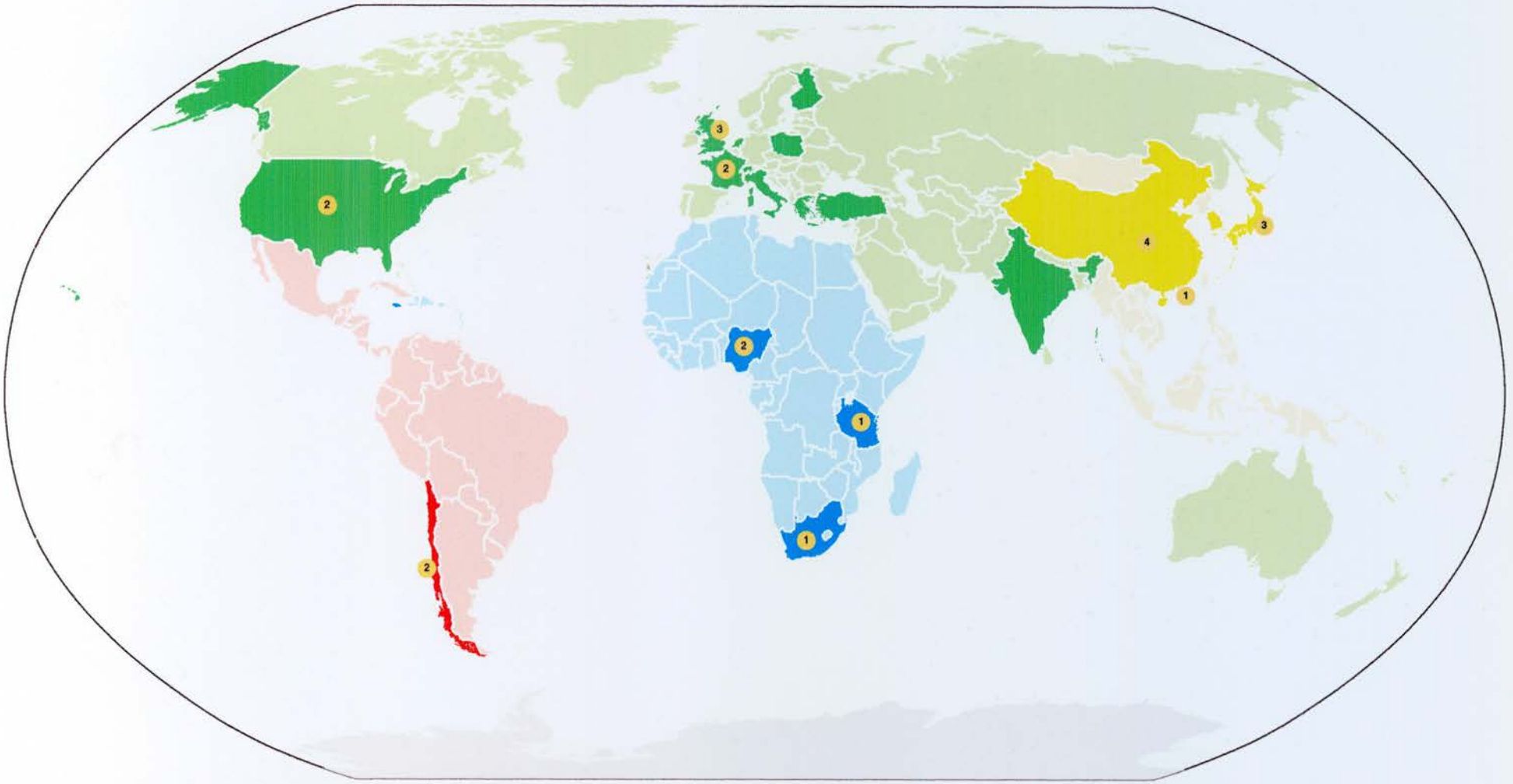


Fibrous Dysplasia: Maxillary Case 3

Note: the unusual root shape - Possible resorption?

Figure 3.

Fig.3



Map 4. Fibrous Dysplasia: Global distribution of 31 Systematic Review-included series of cases coloured according to group

Map 4

The peak decades for the SR were the second and third with 35% and 31% respectively; males accounted for 60% and 55% respectively, although overall they accounted for 44%. No males were observed over the fifth decade. Comparing the first 3 decades with the later decades revealed that there were significantly more males in the earlier decades ($X^2 = 12.58$; 1df; $P < 0.001$). Additionally, Table 7.6 has significantly fewer males than the rest of the SR ($X = 8.33$; 1df: $0.01 > P > 0.001$). Table 7.6 included slightly more Western reports, most were small; the reason for this is unclear.

Table 7.8 compares the present study with the rest of the SR. The higher proportion of males in the present study (females predominated; 11 cases) was not significantly greater than for that for the SR in which females predominated. The present study displayed no significant difference with regards to its predilection for the mandible, whereas those in the SR tended to be more frequently sited in the maxilla.

Location of at least one of the lesions of sextant in the SR was specified in 73 out of 106 cases in 7 reports (Table 7.5); the remaining 33 cases were presumed to have affected both anterior and posterior sextants. Although there was no difference between the present study and the SR, the greatest predilection for the posterior mandible was in the African reports in contrast to the posterior maxilla in Oriental ($X^2 = 23.88$; 3df; $P < 0.001$). No meaningful statistical comparison could be made between the Africans and Western reports, because the latter was represented by a single small report (Garau et al., 1997). There is no difference between the jaws for

cases involving anterior and posterior sextants and those affecting only one (X^2 = 0.15; 1df: $P > 0.05$).

There was no difference between the present report and the rest of the SR with regards to recurrence; it was very low for both.

With regards to predominant radiographic features (Table 7.7), there are no significant differences in radiological presentation between the present study and those SR reports also reporting predominant features (Table 7.8).

All lesions in the present study and the SR exhibited buccolingual expansion (Figure 3.) The frequency of displacement of the inferior border of the mandible was the similar for the present study and the rest of the SR. Three in the present study were also associated with its thinning. Displacement of adjacent roots occurred in 10 cases and did not differ from the rest of the SR. Almost all maxillary lesions in the present expanded upwards into the maxillary antrum; this did not differ in frequency from that observed in the SR. The lamina dura was absent in all cases in which FD affected a dentate area.

Table 7.8 clearly displays that, with the exception of root resorption (atypical; could be very abnormal root development), there is no difference in clinical and radiological presentation between the Hong Kong series and the rest of the SR.

Table 7.8. Fibrous Dysplasia: Chi-square statistics

Feature	Hong Kong	Rest of SR	X^2	Deg. free	P
Gender:Male:Female	10:11	273:294	0.00	1	> 0.05
Albright's Syn: Yes:No	1:20	33:734	0.02	1	> 0.05
Cranio-facial: Yes:No	1:20	50:717	0.12	1	> 0.05
Jaw: Mandible:Maxilla	13:9*	227:333	2.08	1	> 0.05
Swelling:Yes:No	18:3	149:8	2.55	1	> 0.05
Pain: Yes:No	2:19	32:125	1.40	1	> 0.05
Incident.Find:Yes:No	2:19	2:32	0.29	1	> 0.05
Recur:Yes:No	2:19	17:197	0.06	1	> 0.05
Radiolucent:Yes:No	0:22*	13:221	1.26	1	> 0.05
Ground Glass: Yes:No	13:9*	78:126	3.37	1	> 0.05
Peau d'Orange:Yes:No	3:19*	3:84	3.58	1	> 0.05
Sclerosis; Yes:No	1:21*	16:217	0.19	1	> 0.05
Other: Yes:No	5:17*	59:175	0.09	1	> 0.05
Fusiform:Yes:No	13;9	63:70	1.09	1	> 0.05
Multilocular:Yes:No	0:22*	3:28	2.43	1	> 0.05
Expansion:Yes:No	22:0*	159:0	0.00	1	> 0.05
LowBord.Mand:Yes:No	5:7	5:3	0.00	1	> 0.05
AntralInvolve:Yes:No	11:0	11:0	0.00	1	> 0.05
ToothDisplace:Yes:No	10:10	12:30	2.70	1	> 0.05
RootResorpt:Yes:No	2:18	0:113	11:50	1	<0.001

Abbreviations and Note: *, 22 jaws in 21 patients; AntralInvolve, antral involvement; Assoc w teeth, associated with teeth; Incident.Find, incidental finding; Dg.Fre, degrees of freedom; LowBord.Mand, lower border of the mandible; Predom.Radio.present, predominant radiological presentation; RootResorpt root resorption /displacement; SR, systematic review; ToothDisplace, tooth displacement.

DISCUSSION

A striking aspect of this SR is that two-thirds of reports, identified as potential candidates for inclusion, were excluded. The majority were excluded because they failed to use the correct histopathological and radiological features. Although the majority of these reports were derived from medical centres some oral and maxillofacial reports were also among them. Some of the latter were published before the publication of the first edition of the WHO classification, others

particularly the Latin-American reports used Schajowicz (1993) WHO classification of bone tumours. An important reason for this may be that Schajowicz was the head of the 'WHO Collaborating Centre for the Histological Classification of Bone Tumours' based in Buenos Aires in Argentina. Extragnathic FD has quite a different radiological presentation and differential diagnosis.

The results for the Hong Kong population in this study will be discussed in relation to the clinical findings, age and radiology that emerged from the systematic review of the 788 cases. Although the mean age of 27 years in these patients was higher than that of the overall mean of 24 shown in Table 7.5, when prior awareness is taken into account then the mean age falls to 20 years, it is closer to the other reports in Table 7.6 where it can be seen that the lesion occurs most often in the second decade. Although one patient in the fifth decade in the present report (Mandibular Case 12) had remained static for the 15 years after surgery in the third decade does confirm the essentially hamartomatous nature of this lesion, Waldron and Giansanti (1973) considered that some cases of FD were neoplastic. Nevertheless, at least one report, Yetsier and co-authors (2006), considered trauma as a contributing factor; this amounted to 3 out of 26 cases and included road accident, nose surgery and tooth extraction.

Sakota (1977b) also reported a younger mean age for males (18 (7-38) years to the females' 21 (8 to 40) years). The present study differs from the majority of reports, including other Oriental reports with regards to gender, in that it achieves near parity; Table 7.5 reveals a preponderance of females. Nevertheless, it would

appear that the other Oriental population (Korean; Yoon et al.; 1989) did not differ from other groups in this respect. The report of FD being 'initiated' or 'reactivated' during pregnancy suggests that female sex hormones may play a major role in the predilection of FD of the jaws for females shown in Table 7.5. In this regard we would expect females to be older, but there were no significant difference between genders either upon first presentation at PPDH or when adjusted for prior awareness in the present report. Although, this may be in part ascribed to this report containing not enough cases, the present report is the tenth largest in the SR. Nevertheless, sample size is important and is one of the issues SR was developed to overcome by its synthesis of suitable reports. Although, other reports did not compare the ages between genders, females with FD were observed significantly more frequently in the older decades (Table 7.6).

The majority of lesions occurring in the jaws in the present study principally presented as a swelling which was reflected by the expansion of the affected bone seen on the radiographs. This finding is consistent with the SR in which clinically apparent swelling (Table 7.5) and radiographically apparent expansion (Table 7.7) were present in 94 and 100% of cases respectively. The expansion of the mandible involved not only the lingual and buccal plates but also the lower border.

Akintoye and co-authors (2004) report based on syndromic FD is potentially valuable, because it is based on independent corroboration of a diagnosis of FD, multiple bone involvement and endocrinopathies. This type of study should display the whole range of features, which may be associated with FD. They included a

number of cases in which they determined were 'well-defined'; these cases were rather the 'mixed' type. Although they were unable to determine any association between the radiological pattern and endocrinopathy or age, they did not appear to have determined whether there were any other radiological features, which could also be associated with these well-defined cases. Furthermore, their report contained two comments, which severely compromise the value of their report as a radiology report as they purport it to have been. They wrongly excused the apparent absence of radiolucent pattern in the maxilla as due to the 'masking' of it by the translucent maxilla. If this was their meaning then it is wrong because even soft-tissue lesions such as mucosal antral cysts (MACs; MacDonald-Jankowski; 1993a and 1994) are readily visible by being 'silhouetted' against an air-filled cavity. Furthermore, they reported that the inferior dental canal was obscured by the increased density of the bone; this is again wrong.

Terminology

It is clear that merely confining a SR to the English language does not guarantee clarity of understanding of the author's intentions. This becomes particularly pertinent with regards to a feature that is so crucial such as the margin definition, which allows the ready identification of FD from other FOLs, in particular the COF; the former is poorly-defined whereas the latter is well-defined (Eversole et al., 1972). The reports by Williams and Faccini, (1974) and Karja and Rasasen, (1972) illustrate this. They did not directly report the margins, but may have referred to it obliquely by the term "diffuse opacity". The meaning of "diffuse opacity" could

either refer to the margins or to the 'ground glass' appearance. The easiest approach would be to exclude both, but the overarching aim was to include as many SR-includable reports as possible or as much of them as possible. The matter was resolved in the Karja and Rasasen (1972) report by the fact that they clearly expressed the COFs being as "well-defined", whereas this could not be done for Williams and Faccini's (1974 report, which was excluded.

Radiological description

The most common radiographic presentation of FD in the present study was a poorly-defined, ovoid (fusiform) area of dysplastic bone that exhibited a `ground glass' appearance.

The original reasoning behind the importance of marginal definition was developed by Sherman and others (Sherman and Sternbergh, 1948; Sherman and Glauser, 1958) and reaffirmed by Eversole and co-authors (1972); diffuse lesions are dysplastic and well-defined lesions are benign neoplasms. The criterion used in the present report to determine margin-definition was that of Slootweg and Muller (1990). Its application confirmed the poorly-defined nature of the dysplastic lesions in the present study in contrast to the generally well-defined neoplastic COFs in the same community. Waldron and Giansanti (1973) observed that the anterior border of maxillary lesions was well-defined when displayed on a panoramic radiograph. They dismissed this as being a radiographic artefact since neither the occlusal film showed it nor surgery substantiated it. Because this feature could not be observed in

panoramic radiographs in the present study, it would suggest that the continuous moving centres of focusing in the more advanced units have largely eradicated this problem.

The bone pattern may vary not only between different films (for instance, 'ground glass' on screen film and 'peau d'orange' on direct intra-oral film (Cooke, 1957) but also between different parts of the same radiograph (Waldron and Giansanti, 1973). Figure 3 of the present study displayed these features. The variation in density within a radiograph may indicate that different areas of the lesion mature at different times. Although this is supported by Eversole and co-authors' (1972) observation that one case changed from woven to lamellar bone within 2 years, Cooke (1957) did not observe radiographic changes in comparable films over an interval of 10 years.

Other radiological features that could supplement the diagnosis of FD.

In the present study 6 of the posterior mandibular lesions showed a marked downward displacement of the inferior dental canal and only 2 displayed an upward displacement. This finding disagrees with Petrikowski and co-authors (1995), who did not find a single case of downward displacement. Indeed, they suggested that the upward displacement of the inferior dental canal was a unique characteristic of FD. This difference may reflect the different ethnic origin of the 2 studies; Petrikowski and co-authors' (1995) was of a Canadian community, presumably largely based on white patients, whereas almost all of those of the present study were Hong Kong

Chinese. Nevertheless, this phenomenon of upward displacement of the inferior dental canal should be considered for further evaluation as a potential diagnostic sign of FD as the 'tennis racket' is to the odontogenic myxoma (MacDonald-Jankowski, 2002).

The predilection for the right side was observed both by Jacobsson and co-authors (1975) in their 15 Swedish mandibular cases and also by the earlier study on FD in this largely Chinese population (MacDonald-Jankowski, 1999). This predilection, as MacDonald-Jankowski (1999) suggested, may disappear in a larger sample, indeed as it did in the present study, a larger study within the same community. Furthermore, in Jacobsson and co-authors' (1975) report only 4 female cases encroached on the midline. In the present study, FD crossed the midline in only 2 males.

Although Jacobsson and co-authors (1975) reported spontaneous remissions of the recurrent episodes of growth with simultaneous pain and swelling and an occasional elevated ESR, there appears to be no reported spontaneous involution of FD. Therefore, the lesion has to be reduced by surgery (Edgerton et al., 1985) to improve the patient's appearance and function (Mendelsohn et al., 1984) occasionally it may be employed to alleviate pain or ocular disturbances (Bessho et al., 1989). In the present series one mandibular lesion treated surgically had recurred once 16 years earlier, 15 years after the initial procedure. This would suggest that life-long or at least long-term follow-up is required. This is borne out in other SR-included reports.

Ten cases of tooth displacement were observed in the present study. Tooth displacement was also reported by Waldron and Giansanti (1973). The lamina dura was absent in all cases in the present series where assessment was possible. In addition to the upwardly displaced inferior dental canal, Petrikowski and her coworkers (1995) suggested that the loss of lamina dura could be used as an ancillary diagnostic feature for FD.

The apparent 'root resorption' is unusual and may reflect defective root formation, which is highly feasible because this would have taken place during the FD's early growth. Normally, root resorption is very clear radiographically, such as the COF case in Figure 2. The only indisputable evidence of root resorption as displayed in Figure 3 would be further root loss on subsequent radiography, or images taken earlier displaying more root. Furthermore, the presence of root resorption or abnormal roots may merely indicate a variant form or associated lesion.

Recurrence and reactivation

A point of contention that the present author determined with regards to FD was differentiating 'recurrence' from 'reactivation', which is not a merely of academic interest as reactivation is more likely to affect a female, whereas recurrence on present evidence is presumed to affect both genders equally. Often this was not possible and undoubtedly some cases of FD, which were reactivated, were instead reported as recurrences. The term 'recurrence' is applied to a lesion's recidivism following treatment that generally aims to be a complete cure. This treatment in an

oral and maxillofacial context is usually surgical, although drugs (such as antibiotics etc) and radiotherapy have important roles. When surgery is applied it endeavours to excise the entire lesion, but this is not always appropriate. FD is one of those few lesions in which complete excision is inappropriate, although it has to be acknowledged that this does happen in various parts of the world particularly in non-oral and maxillofacial head and neck units (Yeow and Chen, 1999 and Wu and co-authors, 2005). Generally FD of the jaws is biopsied, particularly the monostotic and craniofacial forms, in order to confirm fibro-osseous nature of the clinical and radiological diagnosis of FD (or COF). These biopsies are acquired for diagnosis and not to cure, they can potentially induce further growth, although this has so far not been published with regards to the jaws. In the absence of treatment FD can become reactivated as a result of a life event, such as pregnancy. Although such cases have been reported, their more general manifestations within a case series has not been fully appreciated, partly due to an absence both of very long term follow-up of a large group of cases and the routine taking of gynaecological histories within a oral and maxillofacial context.

Long-term follow-up.

Although according to various authorities, including Waldron (1993) the majority of cases 'burn out' in early adulthood when skeletal maturity has been reached, according to Eisenberg and Eisenbud (1997) there are no studies of FD cases followed up over a long period to substantiate that view. Their contention is supported by later recurrence or reactivation in a small number of FD lesions

followed over a long time, such as a report of two White cases (Sachs, 1997) and one Indo-Caucasian case (MacDonald-Jankowski, 1999). Other cases of FD which have either been reactivated or first activated by pregnancy, suggesting that sex hormones could influence at least some of them; Daly and co-workers' (1994) case of a 25 year-old pregnant Chinese female who became blind in the left eye due to a re-activated or increased-activity craniofacial FD. Jacobsson and co-workers (1976) reported that of their 15 cases of FD reporting recurrent episodes of which 11 were females (6 likely to be in their menarche) only one experienced exacerbations, which appeared to coincide with menstruation, and could be subdued by progesterone. Henry (1969) reported reactivation of FD in two of his patients during pregnancy.

Furthermore, a number of cases continue to grow into adulthood or first present clinically in adulthood (Sakamoto et al., 1999; Garau et al., 1997). Sakamoto and co-workers (1999) report 6 of their 62 Japanese cases of FD presenting in the seventh and eighth decades. Garau and co-authors (1997) reported that 9 out their 12 cases of gnathic FD presented in Italians over 20 years of age; 2 in the seventh and eighth decades. It is possible that these reports may merely reflect the ages the lesions were first detected, diagnosed and recorded rather than a later age of commencement of growth. A late detection of a long-standing lesion is entirely possible because many cases of FD are painless (MacDonald-Jankowski, 1999).

Although long term follow-up of series of cases is rare, Jacobsson and co-workers followed-up for 13 years 15 cases of FD (all affecting the mandible)

displaying recurrent episodes of growth with simultaneous pain, swelling and occasional elevated erythrocyte sedimentation rate (ESR) and fever.

It was clear from Sissons and Malcolm's (1977) autopsy of a woman who had lived with her FD since it was diagnosed 80 years earlier that most of the dysplastic bone retains the non-lamellar appearance observed in young patients.

Risk of Blindness with FD of the jaws.

Fibrous dysplasia affecting the maxilla almost always involves the antrum (Table 7.5), which it not only occasionally obliterates but also, displaces the orbital floor upwards; this was apparent in Maxillary Case. 4; this maxillary lesion clearly encroaches upon the orbital cavity. FD cases, as would any other expansile lesion, such as COFs, arising in close proximity to the orbit and the optic canal clearly pose a major risk to vision; Boysen and co-authors (1979) reported displacement of the eye in 2 out of 5 extragnathic FD cases, but 7 out of 10 extragnathic COFs. Although 2 cases out of the 788 SR-included cases of FD affecting the maxilla were associated with ocular defects, one with an atrophic eye and the other with a loss of vision, the evidence of FD as the direct cause of these was clearly lacking. The latter case was of FD confined to the mandible. Yetiser and co-authors (2006) surmised that the loss of vision was "probably caused by (an) accompanying meningioma." On the other hand, Yetiser and co-authors (2006) reported 2 cases of proptosis out their 18 extragnathic cases. Proptosis was not infrequently reported in extragnathic FD. Although proptosis itself is not a direct threat to vision, it does indicate involvement

of an aspect of the ocular apparatus. Katz and Nerad (1998) also presented a mandibular FD case causing visual impartment very indirectly by an intra-operation infarct of the visual cortex during an operation for the mandibular lesion. Therefore, although FD poses an undoubted risk to vision, the SR would indicate that for those lesions affecting the jaws, this risk is very low, even although some cases of the present study, particularly if CT is used, extended right up to the floor and even displaced it (MacDonald-Jankowski et al., 2004b). The out-of-region referred Indian patient, excluded from the present study, presented with ocular symptoms.

Although this SR of reports of FD cases primarily affecting the jaws did not reveal a particular propensity to cause ocular disturbances, this is clearly not the experience of ophthalmologists and otolaryngologists, working on FD cases closer to the eyes and optic nerves. Chen and Noordthoff (1989) usefully divided the head into 4 zones with regards to technical difficulty and seriousness. The jaws were in zone 4 which had minimal impact on vision in contrast to zone 3, the base of the skull, which had the highest impact. Becelli and co-authors (2005) reiterated the severe clinical impact of FD affecting this zone. Of the 20 cases of FD with ophthalmic manifestations, in Katz and Nerad's (1998) report, only 2 were associated with the maxilla as the primary location, although it was reportedly part of wider disseminated disease in most other cases. Furthermore, at least one of their cases affecting the frontal bone did not look-like FD from an oral maxillofacial or dental perspective.

Pathological fractures within cases of FD of the jaws.

Pathological fractures of biopsied FDs affecting the jaws are very rare occurrences in contrast to those affecting extragnathic weight-bearing bones; Henry (1967) reported that, while 12 cases out of 27 cases of FD affecting the long bone displayed pathological fractures, only one case was observed in the 12 affecting the jaws, this was significant ($X^2 = 7.73$; 1df; $0.01 > P > 0.001$). Although this Hong Kong community would appear to be the first SR-included report in which a case of a pathological fracture occurring in FD of the jaws is reported, it is likely that the previous surgery would have contributed to it. Pathological fracture of the dysplastic jaws, while frequent in other bones affected by FD (Stewart and Gilmer, 1962), has not been reported in the jaws (Daramola et al., 1976). Furthermore, Leet and co-authors (2004) reported that "the occurrence of extremity fractures in FD peaks between 6 and 10 years of age and declines thereafter", as can be seen from Table 7.7, only a small proportion of FD cases appear in the first decade, therefore, the risk of fracture resulting from an appropriately indicated and sited biopsy should be negligible.

Many of the FDs in the present study were of sufficient size and classical in their clinical and radiological presentations that a sole diagnosis of FD was offered in nearly every case. Sakota (1977b), the only other report to consider the clinician's provisional diagnosis, reported that 34 out of 49 FD cases were correctly identified; only 4 FDs were misdiagnosed as OFs, whereas only 2 of his 13 COFs were provisionally diagnosed as FDs. Many of these errors could have resulted from the

confusion about the FD-COF dichotomy and the central role of radiology that appeared to have been widespread in the 1960s and early 1970s (see Table 7.5.) when these cases first presented. This poses the question as to whether a biopsy was really necessary for these cases. Biopsies are no longer routinely performed for other lesions not only for FCODs, but also the majority of small focal CODs (which may be early COFs), or idiopathic osteosclerosis.

CONCLUSIONS

1. Although the SR-included reports were largely lacking in detail, with particular regard to the radiology, the overall review of all the relevant literature clearly indicated that the FD and COF are very different lesions upon which the main diagnosis is the definition of the margin. For those reports, which recognize this central tenet, there is an absence of any reported difficulty or error arising from its application. This does not mean that this tenet is infallible; it simply means that it is robust and a clinician can rely upon it. What is still lacking is really long-term follow-up and detailed reporting. Only these two together can assist the clinician to determine whether there are clinical and/or radiological features which could indicate that a particular patient is more likely to experience recurrences or reactivations. Jacobsson and co-authors' (1975) report would indicate that FD has frequent relapses in at least some patients.

2. FD affecting the jaws in this largely Chinese series of cases displayed features that were similar to those in almost all other reports in the SR. The radiology

of these lesions contributed not only to the accuracy of the diagnosis but also to the definition of the extent of the lesion. The latter is important, because although there are only 2 SR-included cases (those arising primarily from the alveolar process of the maxilla) very remotely associated with ocular defects, 1 case arising from the jaws excluded from the SR but reported in present author's CT report (MacDonald-Jankowski et al., 2004b) was associated with ocular signs. Similarly, the pathological fracture and malignant transformation into osteogenic sarcoma do not appear as features of reported series of FD cases affecting the jaws.

3. The apparent root resorption was unexpected, but it is not the classical root resorption associated with benign processes. It may reflect defective root formation. This is feasible as it is clear that most of the Hong Kong cases began in adolescence when root formation of posterior sextant teeth would normally be underway.

Chapter 8.

Discussion: COMPARING SYSTEMATIC REVIEWS

Introduction

The foregoing SRs on each of the 4 FOLs that affect the jaws reveal details of their main clinical, and radiological features and also how well documented they are in the literature. The significance of differences in their clinical and main radiological presentations will be discussed. In order to determine deeper patterns within and between the 4 SRs, their reports were divided into 4 global groups based broadly on the fundamental division of the human race; these are Oriental (predominantly represented in this thesis by Chinese and Japanese), African (predominantly Black African, including Jamaica), Western (North America and Europe (including Turkey), Middle East and India), and Latin-American (including Cuba). Although the 'Western' group is predominantly White (Caucasian; classically Europe and the Middle East) it contains significant non-White minorities, particularly from Africa. The sole Indian report was included in the Western group, because 95% of Indians are Caucasian.

Non-English Languages.

The non-English languages of the SR-included reports in the 4 SRs are set out in Table 8.1a and statistically analysed in Table 8.1b. Table 8.1a also compared the 4

FOL SRs to the outcomes of other recent SRs; 3 performed by the present author (odontogenic myxoma, Map 5; ameloblastoma, Map 6; and dentigerous cysts Map 7) and 2 others according to the method he established (Stravopoulos and Katz 2002; Golan et al., 2003). It is clear that there is no significantly greater inclusion of non–English language SR-included reports within the 4 FOL SRs (Table 8.1b); indeed, the FocCOD SR-excluded reports were all English language, whereas 3 of the 10 SR-included reports were in Japanese. This would suggest that all SRs are capturing the similar proportions of non-English language reports, thus reflecting the truly global distribution of these lesions and the scholarship applied to them. The majority of the non-English language SR-included reports for each of the 4 FOLs are Oriental; almost all are in Chinese or Japanese. Although this predilection for Oriental reports between the present author's FOL and non-FOL SRs was not significant, when Oriental, non-Oriental and English reports were compared (a total of 14, 6 and 61 respectively for the 4 FOL SRs and 11, 20 and 98 for the 3 non FOL SRs) this was significant; $X^2 = 5.88$; 2df: $P > 0.05$). Furthermore, a comparison of only the Oriental and non-Oriental for the two groups of SRs was also significant ($X^2 = 5.81$; 1df: $0.05 > P > 0.01$). The Oriental reports were the most numerous except for the FD SR in which the Europeans (including the Turkish and Indian reports) predominated. The differences between COF and FD, and FocCOD and FD, each for Oriental, non-Oriental and English reports, were insignificant ($X^2 = 2.16$ and 4.66 respectively; 2df; $P > 0.05$).

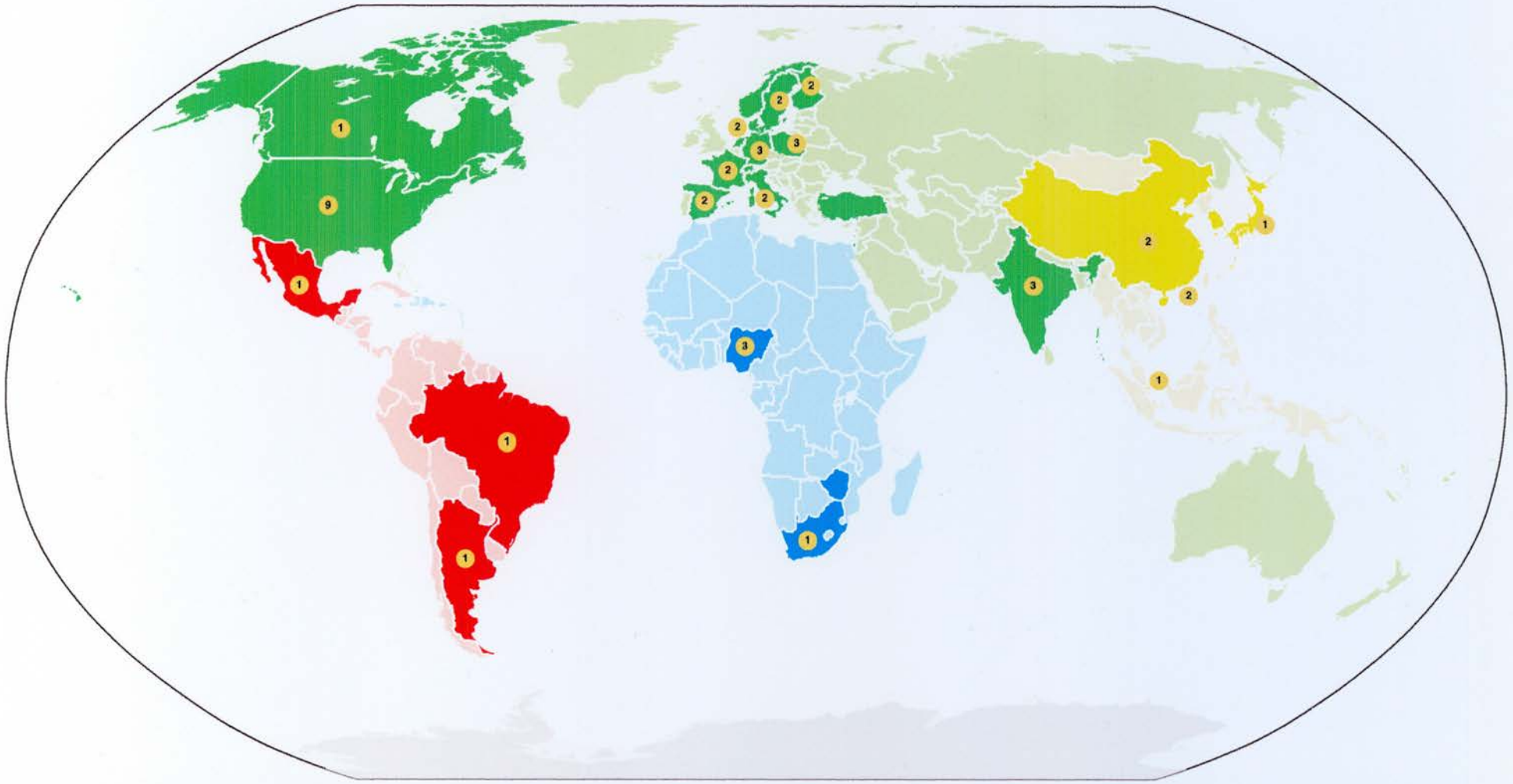
Table 8.1a. Non-English Language Reports included in SRs; comparing 9 SRs

Systematic Review (SR)	Non-English Language Reports included in the SR										Total reports per SR	Total Non-English Reports per SR	% of Non-English Reports per SR
	Romance			Germanic		Other		Oriental/East Asian					
	French	Spanish	Italian	German	Norwegian	Polish	Greek	Chinese	Japanese	Korean			
Florid Cemento-Osseous Dysplasia	1	0	0	0	0	0	0	0	2	0	20	3	11.8
Focal Cemento-Osseous Dysplasia	0	0	0	0	0	0	0	0	3	0	10	3	30.0
Cemento-Ossifying Fibroma	0	1	2	0	0	1	0	2	2	0	27	8	29.6
Fibrous Dysplasia	1	2	1	0	0	1	1	4	2	0	31	11	35.5

Continued on next page

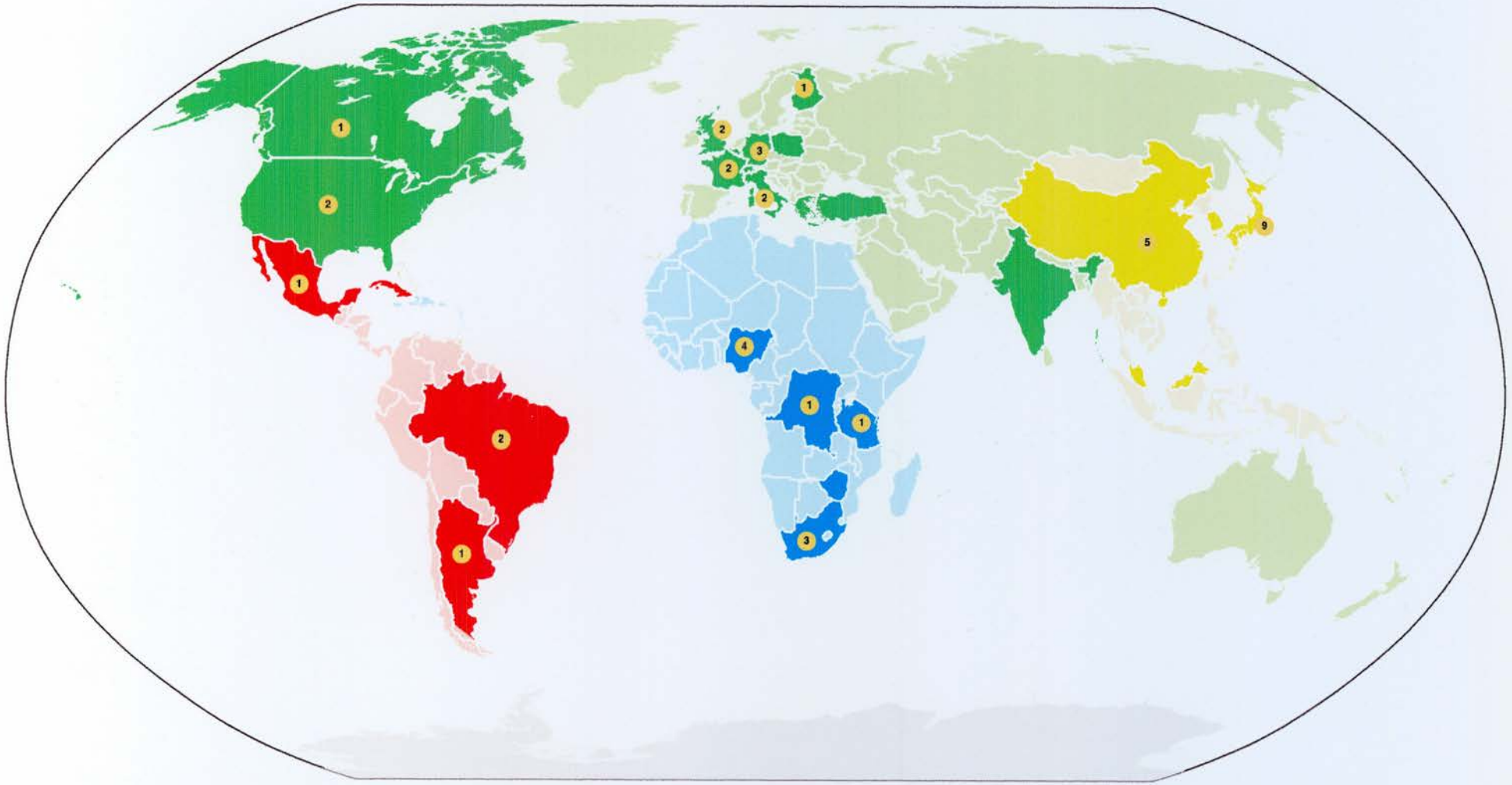
Systematic Review (SR)	French	Spanish	Italian	German	Nor-wegian	Polish	Greek	Chinese	Japan-ese	Korean	**Total reports per SR**	**Total Non-English Reports per SR**	**% of Non-English Reports per SR**
The present author's other SRs													
Ameloblastoma	*1*	*0*	*1*	*2*	*0*	*0*	*0*	*0*	*4*	*0*	*54*	*8*	*14.8*
Odontogenic Myxoma	*2*	*2*	*1*	*2*	*0*	*2*	*2*	*0*	*0*	*0*	*46*	*9*	*19.6*
Dentigerous Cyst	*3*	*2*	*0*	*1*	*1*	*1*	*0*	*1*	*5*	*1*	*29*	*14*	*48.3*
Other SRs expressly based on the present author's method(except for the language restrictions)													
Giant Cell Granuloma	0	0	0	0	0	0	0	0	0	0	6	*0*	*0*
Cleidocranial Dysostosis*	2	0	0	4	0	0	0	0	0	0	17	*6*	35.3

** case series only; in addition to English considered only French and German reports*



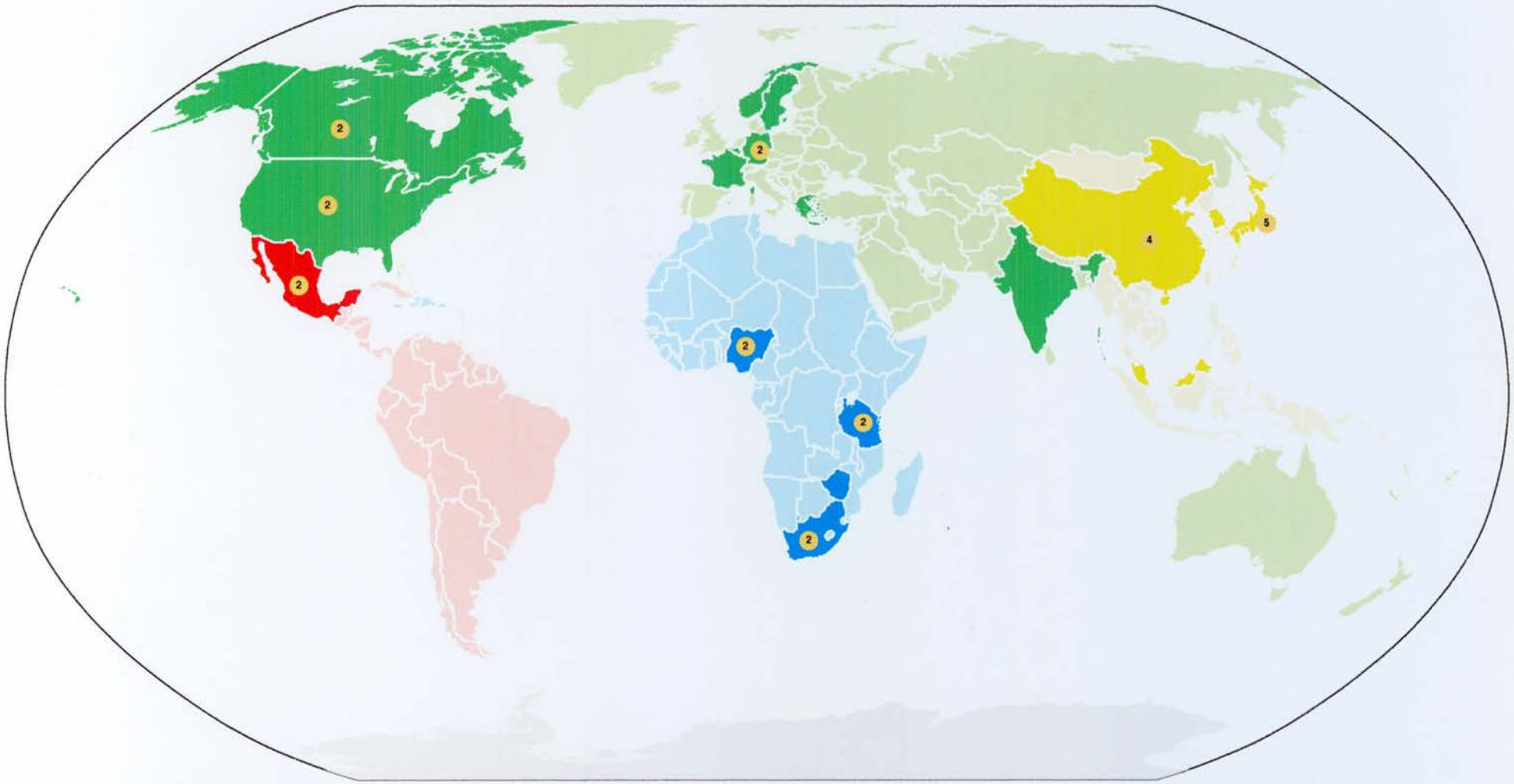
Map 5. Odontogenic Myxoma: Global distribution of 46 Systematic Review-included series of cases coloured according to group

Map 5



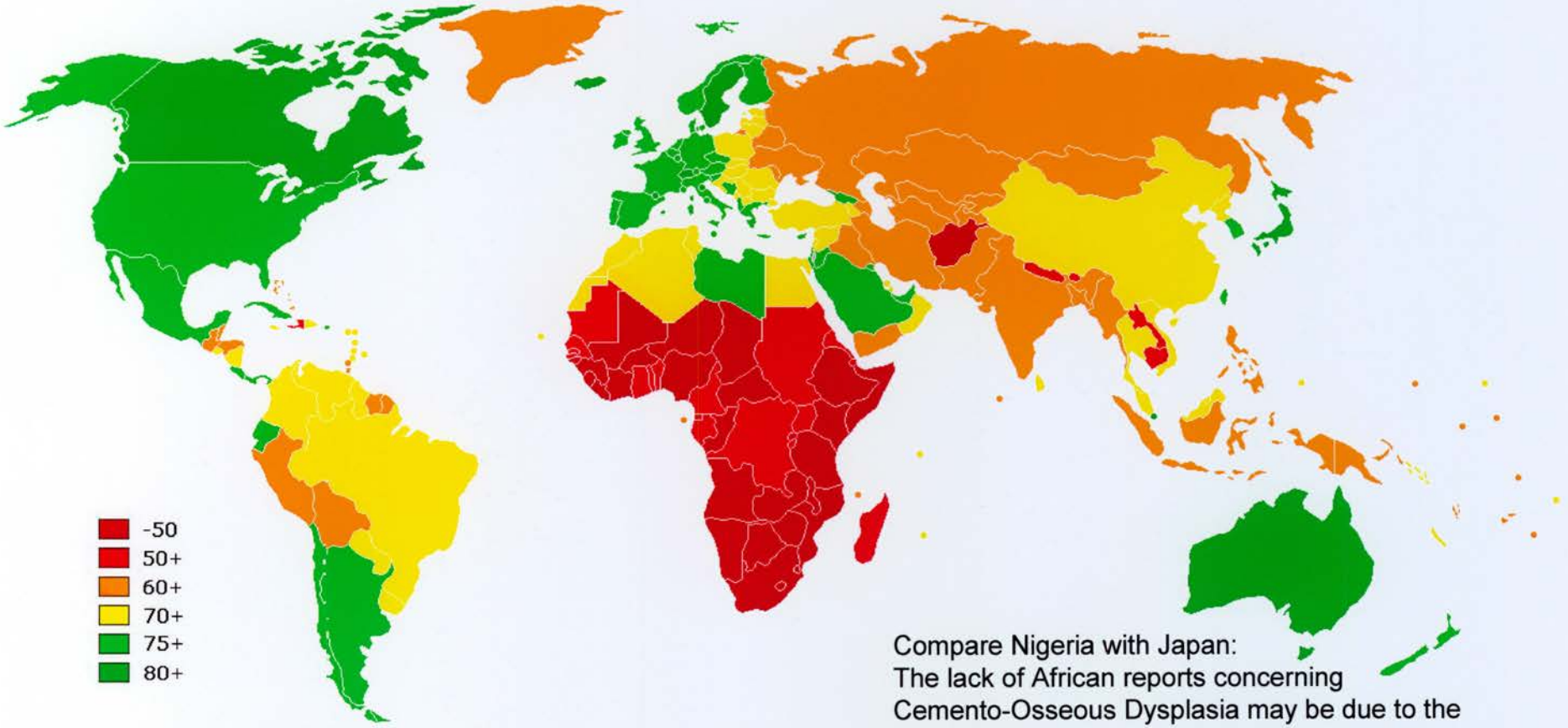
Map 6. Ameloblastoma: Global distribution of 54 Systematic Review-included series of cases coloured according to group

Map 6.



Map 7. Dentigerous cysts: Global distribution of 30 Systematic Review-included series of cases coloured according to group

Map 7.



Compare Nigeria with Japan:
The lack of African reports concerning Cemento-Osseous Dysplasia may be due to the fact that Africans may not live long enough to acquire them

Global Life Expectancy

http://upload.wikimedia.org/wikipedia/commons/6/6e/Life_expectancy_world_map.PNG

Figure 4.

Fig. 4

Table 8.1b. Non-English Language of published SR-included Reports (excluding the present study) Reports

Language Yes:No	FCOD 3:16	FocCOD 3:6	COF 8:18	FD 11:19
FCOD 3:16		1.19	1.27	2.43
FocCOD 3:6	1.19		0.02	0.02
COF 8:18	1.27	0.02		2.38
FD 11:19	2.43	0.02	2.38	

Global distribution of the SR-included reports.

The maps of the 7 lesions display different global distributions. The CODs are largely confined to the Western and Oriental groups, whereas the odontogenic myxoma and ameloblastoma affect all 4 regions, with COF and FD intermediate in their distributions. When these are compared to the map of life expectancy (Figure 4) it is apparent that the CODs, the lesions with the oldest mean age are poorly represented in those regions where life expectancy is low. This may mean that individuals who would be susceptible to CODs may not live long enough to present with them, whereas, those lesions with a younger age of onset are well represented in these areas.

Grounds for exclusion

Approximately 50% of the reports considered for inclusion were eventually excluded for each SR; the exception was the FD SR of which a significant two-thirds were excluded ($X^2 = 8.37$; 3df: $0.05 > P > 0.01$). The exclusions were made mainly on histopathological and radiological grounds.

The number of SR-included reports.

The number of reports included for each of the SRs (Table 8.1a) on important OMF lesions including the 4 FOLs, suggests that the two most clinically significant lesions, the ameloblastoma and the odontogenic myxoma, which can have the most severe outcome (death) and require complete removal, were associated with more SR-included reports whereas the least clinically significant, the FCOD, has minimal severe outcomes provoked fewer. The FocCOD, which was so recently identified, has been the subject of even fewer. The COF, which also requires complete removal to avoid recurrence, is in intermediate rank along with the dentigerous cyst, a common lesion, which is generally surgically treated without any long-term effect on the patient.

The mean number of cases per SR-included report per lesion

The mean number of cases per SR-included report per lesion varies markedly (Table 8.2). Although there is also considerable variation within each group, it is not

statistically significant due to the wide standard deviations reflecting the wide range of the number of cases per report; this is evident when the large but plausible differences between FCOD and FocCOD, and between Oriental and Western FD groups are statistically analysed. This analysis places the apparent incongruity observed when FCOD and FocCOD (the 2 lesions most commonly associated in Black patients resident in Western communities and by reasonable inference with Africans) were lowest for the African group. The lack of significance does not dispel this incongruity but rather by highlighting the availability of very few SR-included reports emphases it. Nevertheless, the later establishment of formal oral and maxillofacial services in Africa has not handicapped African representation within the COF and FD SRs. Evidence for the effects of this recent establishment are evident in Table 8.3 with regard to the 'mean number of years covered by the reports'. The Oriental group's 'mean number of years' covered is significantly greater than Africans for COFs. This would suggest that the large number of cases in the African group might reflect more its reservoir of COFs inTable 8.4.

Although the greater number of FocCODs in Table 8.2 reinforces the current view that they are the most common occurring FOL, numbers vary markedly between FocCOD reports.

The significantly greater 'mean number of cases per SR-included report' (Table 8.2) of the Oriental FD group (which reflects 'prevalence') than the Western may reflect both the higher 'mean number of years covered by the report' (Table 8.3) and 'number of cases per hospital per year' ('incidence'; Table 8.4).

The 'number of cases per hospital per year.'

Although the 'number of cases per hospital per year' is not identical to the lesion's 'incidence', as it is likely to include the existing reservoir of disease prior to the establishment of formal oral and maxillofacial services, it does serve as an indicator of the potential annual contribution that the lesion may make to that service's clinical load. Table 8.4 compares the statistical analysis comparing the proportions of the 'number of cases per hospital per year' that can be calculated for each SR-included report in each FOL (SR). There are no significant differences among the 4 global groups of reports permitting the calculations of 'number of cases per hospital per year' and those, which could not (Table 8.5). Table 8.4 displayed the mean 'number of cases per hospital per year'; this could be calculated in the majority of FOLs except the African FocCODs. Only the difference between COF's African and Western groups was significant, suggesting that the 'number of cases per hospital per year' was greater in Africans. The significantly short mean 'number of years covered' (Table 8.3) raises the possibility that this higher 'number of cases per hospital per year' may reflect the pre-existing reservoir of disease. A larger 'number of years covered' permits the initially large numbers occasioned by the reservoir to become increasingly diluted with each passing year, until the 'number of cases per hospital per year' approaches, but never achieves, truly 'incident' levels.

Table 8.2. Mean number of cases per SR-included report

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin American (Number of reports)	Western (Number of reports)
FCOD	9.35 sd 8.22 (20)	8.38 sd 5.10 (8)	4.67 sd 3.06 (3)	N/A	11.78 sd 10.93 (9)
FocCOD	57.00 sd 75.39 (10)	23.40 sd16.99 (5)	63 (1)	N/A	97.50 sd 112.19. (4)
COF	24.96 sd 26.04 (27)	34.50 sd 40.68 (8)	21.33 sd 10.86 (5)	8.50 sd 4.95 (2)	23.00 sd 20.09 (12)
FD	25.55 sd 29.31 (31)	47.11 sd 33.81 (9)	33.80 sd 39.63 (5)	4.00 sd 2.83 (2)	12.73 sd 13.14 (15)

Significant differences only	
FD: Oriental and Western	t = 2.92: 22df: 0.01 > P > 0.001

Table 8.3. Mean number of years covered by the reports

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin America (Number of reports)	Western (Number of reports)
FCOD	17.67 sd 8.73 (12)	21.00 sd 10.39 (6)	17.50 sd 3.54 (6)	N/A	12.75 sd 6.40 (4)
FocCOD	16.20 sd 10.64 (5)	17.25 sd 11.98 (4)	N/A	N/A	12.00 (1)
COF	18.89 sd 10.23 (19)	21.00 sd 8.05 (6)	10.83 sd 5.95 (6)	36.00 (1)	22.00 sd 11.10 (6)
FD	14.96 sd 8.74 (23)	22.00 sd 10.37 (6)	11.80 sd 6.10 (5)	10.00 (1)	13.00 sd 7.60 (11)

Significant differences only	
COF: Oriental and African	t = 2.49: 10df: 0.05 > P > 0.01

Table 8.4. Mean 'number of cases per hospital per year'

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin American (Number of reports)	Western (Number of reports)
FCOD	1.09 sd 1.49 (12)	0.61 sd 0.60 (6)	0.26 sd 0.19 (2)	N/A	2.23 sd 2.22 (4)
FocCOD	5.42 sd 8.24 (5)	1.78 sd 1.42 (4)	N/A	N/A	20.00 (1)
COF	1.82 sd 1.78 (19)	1.57 sd 1.15 (6)	3.05 sd 2.44 (6)	0.03 (1)	1.13 sd 1.02 (6)
FD	1.62 sd 1.68 (23)	1.87 sd 1.52 (6)	3.22 sd 2.57 (5)	0.03 (1)	0.89 sd 0.56 (11)

Significant differences only	
COF: African and Western	t = 2.56: 10df: 0.05 > P > 0.01

Table 8.5. The proportion of reports which permit calculation of 'Number of cases per hospital per year'

	All Yes: No	Oriental Yes: No	African Yes: No	Western Yes: No	Latin American Yes: No	Significance of Differences
FCOD	12:8	6:2	2:1	4:5	N/A	$X^2 = 1.70$: 3df: P>0.05
FocCOD	5:5	4:1	0:1	1:3	N/A	$X^2 = 0.38$: 3df: P>0.05
COF	19:8	6:2	6:0	6:5	1:1	$X^2 = 3.97$: 3df: P>0.05
FD	23:8	6:3	5:0	11:4	1:1	$X^2 = 1.85$: 3df: P>0.05

Although, the relative paucity of series of cases of FCOD from Africa could be explained away by the relative ease of their diagnosis purely on radiological grounds and thereby their absence in the histopathology case files from which many such reports are derived. This reason cannot account for the relative absence of FocCODs, because they have a more extensive differential diagnoses due to their more non-specific radiological presentation.

Furthermore, both FDs and COFs displayed falls in the 'number of lesions per hospital per year' before and after 1990. The year 1990 was chosen arbitrarily as a round year close to the medium year of publication of the reports in the ameloblastoma SR. it also occurs nearly 2 decades after the WHO's first edition on odontogenic neoplasms (Pindborg et al., 1971), which could be expected to establish from the time of publication a global awareness of all the lesions it addresses. Indeed its preface stated that its intent is to "promote the adoption of a uniform classification." A rise in the 'number of ameloblastomas per hospital per year' since 1990 (one of the more common odontogenic neoplasms; Macdonald-Jankowski et al., 2004c) was associated with an increase in reports from developing nations addressing their reservoirs by recently established of oral and maxillofacial services in contrast to the longer established services of developed nations which had largely absorbed their reservoirs prior to the 1990. Hence, their lower 'number' now reflects more the disease's annual incidence in that community. This may be the reason why so many FDs in the present study were already long known to their patients.

Gender

Table 8.6a displays no statistical difference between the proportions of SR-

Table 8.6. Gender

a. Reports

GENDER Yes:No	FCOD *16:4*	FocCOD *8:2*	COF *19:8*	FD *22:9*
FCOD *16:4*		0.00	0.56	0.52
FocCOD *8:2*	0.00		0.34	0.33
COF *19:8*	0.56	0.34		0.00
FD *22:9*	0.52	0.33	0.00	

b. Cases

GENDER Male:Female	FCOD *5:147*	FocCOD *55:393*	COF *145:372*	FD *273:294*
FCOD *5:147*		10.18	74.94	136.89
FocCOD *55:393*	10.18		37.96	147.32
COF *145:372*	74.94	37.96		30.60
FD *273:294*	136.89	147.32	30.60	

Table 8.6c: Gender: cases

GENDER	All Male: Female	Oriental Male: Female	African Male: Female	Western Male: Female	Latin American Male: Female	Significance of Differences
FCOD	5: 147	3: 50	0: 14	2: 83	0: 0	$X^2 = 1.78$: 3df: P>0.05
FocCOD	55: 393	16: 99	4: 59	35: 235	0: 0	$X^2 = 2.46$: 3df: P>0.05
COF	145: 372	62: 167	14: 28	66: 168	3: 9	$X^2 = 0.79$: 3df: P>0.05
FD	273: 294	154: 163	50: 68	62: 62	7: 1	$X^2 = 7.07$: 3df: P>0.05

Table 8.7a. Mean age at first presentation

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin American (Number of reports)	Western (Number of reports)
FCOD	50.69 sd 8.41 (13)	50.75 sd 7.50 (4)	49.00 sd 6.56 (3)	N/A	51.50 sd 10.78 (6)
FocCOD	44.50 sd 6.12 (6)	47.25 sd 5.62 (4)	N/A	N/A	39.00 sd 1.41 (2)
COF	30.25 sd 6.73 (16)	33.50 sd 3.42 (4)	19.33 sd 4.62 (3)	33.00 (1)	32.38 sd 4.75 (8)
FD	23.76 sd 5.18 (21)	24.20 sd 6.42 (5)	23.00 sd 3.60 (3)	16.50 sd 3.50 (2)	25.09 sd 4.35 (11)

Significant differences only	
FCOD and COF	t = 7.10: 28df: $P < 0.001$
FCOD and FD	t = 10.40: 32df: $P < 0.001$
FocCOD and COF	t = 4.72: 20df: $P < 0.001$
FocCOD and FD	t = 7.57: 25df: $P < 0.001$
COF and FD	t = 3.20: 35df: $0.01 > P > 0.001$
COF: Oriental and African	t = 4.47: 5df: $0.01 > P > 0.001$

included reports reporting gender, whereas Table 8.6b indicated that there are highly significant differences between them all, particularly between the FD, which displays almost parity, and the FCOD and FocCOD, which are almost completely composed of females. Table 8.6 c. does not reveal any significant difference for gender between the 4 global groups for each lesion.

Age

The mean ages of each lesion at first presentation and for each of the 4 global groups are set out in Table 8.7a Table 8.7b displayed no significant difference between the proportions for the SR-included reports recording mean age at first presentation. The average ages between all 4 FOLs differed significantly and (Table 8.7a) ascended in the following order; FD, COF, FocCOD and FCOD. The only significant difference

Table 8.7b. Mean Age at first presentation

b. Reports

Mean Age Yes:No	FCOD 12:8	FocCOD 6:4	COF 16:11	FD 21:10
FCOD 12:8		0.00	0.00	0.26
FocCOD 6:4	0.00		0.00	0.21
COF 16:11	0.00	0.00		0.43
FD 21:10	0.26	0.21	0.43	

within a FOL was that the Oriental COF group was significantly older than the African COF group. All 4 Oriental reports contributing to this have their mean ages in the 4th decade (Table 6.6). Although, the lower average age for Africans for FCODs than for Orientals was unexpected (49 compared to 51 years respectively), it is consistent with the World Health Organsations's 2005 lower life expectancy for African nations, such as 47.6 years for Nigeria (the source of most African reports) in contrast to the 82.2 years for the Japanese (the source of most Oriental reports). The simple explanation, that most of the population with the potential to acquire this disease dies before it can be manifested, is difficult to support because the Western reports, predominantly populated by patients of African-origin, give the lowest average age of 45 years. This would suggest that other factors are present.

Pre-presenting awareness of FOLs

The age at presentation may not always indicate the precise age the patient

Table 8.8. Pre-presentation awareness of the lesion.

a. Reports

Mean Age Yes:No	FCOD 0:20	FocCOD 0:10	COF 3:24	FD 5:26
FCOD 0:20		0.00	2.44	3.69
FocCOD 0:10	0.00		1.18	1.79
COF 3:24	2.44	1.18		0.28
FD 5:26	3.69	1.79	0.28	

became aware of his/her disease, it is clear from the FD SR and that the patient's pre-presenting awareness could be considerable. Table 8.8 shows no significant difference in the proportion of SR-included reports recording the pre-presenting awareness of the lesions. Only 3 and 5 reports were included in the COF and FD SRs respectively.

The mean duration for FD was 2.7 years and that for COF was 1.1 years. A lack of similar information for the FocCODs may be due to their asymptomatic nature. The influence of awareness on the eventual outcome of these lesions when appropriately managed has not been assessed. Certainly for FD, where no treatment is necessary, it merely may mean that the patient is aware of his/her disease for longer than most of the reports would suggest.

It is clear from the present FD study that many patients were already aware of their lesion, before presenting to PPDH. In some cases it had already been diagnosed and even treated to some extent. Nevertheless, a history of the patient's awareness of the lesion was only available in 2 other smaller reports (Obwegeser et al., 1973; Adekeye et al., 1980). This brings attention to an important difference between the FD and the other SRs with regards to selection criteria. A firm selection criterion for the others was that reports which included excessive number (over 10% of the total number of cases) of recurrent cases that could not be identified and deleted should be excluded from the SR, was not applied to FD unless the recurrent cases failed to give an indication of when they first presented. The principal treatment aim for neoplasms (odontogenic myxomas, MacDonald-Jankowski et al., 2002; ameloblastomas, MacDonald-Jankowski et al., 2004a and b) and dentigerous cysts (MacDonald-

Jankowski and Chan, 2005), which may contain neoplasms (Wang, 1985), is complete removal of the lesion so as to prevent its recurrence. Recurrent lesions were excluded because they are occurring within an area already disrupted not only by the surgery but also by subsequent healing and scarring, which have the potential to change the presentation of the recurrent lesion which in turn would obfuscate the presentation of the primary lesions if the recurrent lesions were included in the SR in large numbers.

Jaw and Sextant affected

Table 8.9a, concerning the affected jaw, does not display a significant difference in proportion of those SR-included reports of each FOL, which recorded the jaw and those which did not. In Table 8.9b the FCOD had been excluded because it commonly affects both jaws. There were a significantly higher proportion of FocCOD than COF cases affecting the mandible. The predilection of FD for the maxilla is obvious. In Table 8.9c COF record significantly more cases recording jaws than FCODs. In the FD SR Oriental reports record significantly more cases with jaws than do Western reports.

Although in Table 8.10a the FocCOD SR-included report recorded the sextant more frequently than those of FD, there were no significant differences between the cases for either jaw. Nevertheless, they both display a similar predilection for the posterior sextants in the mandible in contrast to the COF (Table 8.10b.), which was distributed almost equally between anterior and posterior sextants

for the mandible. Although this would suggest that both FD and FocCODs have a predilection for the posterior sextants, Table 8.10a would indicate that this may not be so for FD as only very few SR-included reports recorded sextant. In Table 8.10c, within the FD SR the Oriental group recorded significantly more sextants than the Western group. This would suggest that the Oriental FDs were smaller at first presentation putting it at odds with the present report. This would suggest that Hong Kong Chinese may report their FDs at a later stage than elsewhere in the Orient.

Table 8.9. Jaw

a. Reports

JAW **Yes:No**	**FCOD** ***13:7***	**FocCOD** ***7:3***	**COF** ***19:8***	**FD** ***26:5***
FCOD ***13:7***		0.06	0.15	2.40
FocCOD ***7:3***	0.06		0.00	0.83
COF ***19:8***	0.15	0.00		1.43
FD ***26:5***	2.40	0.83	1.43	

b. Cases

JAW **Mandible:Maxilla**	**FCOD** **N/A**	**FocCOD** **332:55**	**COF** **282:102**	**FD** **240:336**
FCOD **N/A**				
FocCOD **332:55**			18.33	252.94
COF **282:102**		18.33		187.73
FD **240:336**		252.94	187.73	

Table 8.10. Sextant

a. Reports

Sextant Yes:No	FCOD 9:11	FocCOD 6:4	COF 10:17	FD 6:25
FCOD 9:11		0.60	0.30	3.81
FocCOD 6:4	0.60		1.62	6.16
COF 10:17	0.30	1.62		2.34
FD 6:25	3.81	6.16	2.34	

b. Cases

Sextant MANDIBLE Anterior:Posterior	FCOD N/A	FocCOD 58:231	COF 61:71	FD 4:24
FCOD N/A				
FocCOD 58:231			30.58	0.56
COF 61:71		30.58		9.82
FD 4:24		0.56	9.82	

Sextant MAXILLA Anterior:Posterior	FCOD N/A	FocCOD 13:36	COF 14:29	FD 10:37
FCOD N/A				
FocCOD 13:36			0.42	0.38
COF 14:29		0.42		1.42
FD 10:37		0.38	1.42	

Table 8.9c. Mean number of cases recording jaws

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin American (Number of reports)	Western (Number of reports)
FCOD	9.85 sd 8.90 (13)	9.20 sd 5.02 (5)	5.00 sd 4.24 (2)	N/A	12.00 sd 12.28 (6)
FocCOD	70.88 sd101.29 (8)	19.00 sd 9.06 (5)	N/A	N/A	157.33 sd133.42 (3)
COF	19.35 sd 15.90 (20)	19.00 sd 6.71 (5)	17.00 sd 10.98 (4)	9.00 sd 4.24 (2)	22.89 sd 22.06 (9)
FD	21.27 sd 28.86 (26)	48.33 sd 37.06 (6)	30.75 sd 45.08 (4)	4.00 sd 2.83 (2)	9.43 sd 6.39(14)

Significant differences only	
FCOD and COF	t = 3.39; 30df: 0.01 > P > 0.001
FD: Oriental and Western	t = 2.56; 18df: 0.05 > P > 0.01

Table 8.10c. Mean number of cases recording sextants

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin American (Number of reports)	Western (Number of reports)
FCOD	9.25 sd 7.32 (8)	9.33 sd 7.09 (3)	6.00 (1)	N/A	10.00 sd 9.34 (4)
FocCOD	56.33 sd 91.76 (6)	19.00 sd 8.48 (5)	N/A	N/A	243.00 (1)
COF	16.70 sd 17.56 (10)	16.00 sd 5.00 (3)	7.00 (1)	8.50 sd 4.94 (2)	23.75 sd 27.52 (4)
FD	13.38 sd 8.86 (8)	26.00 sd 7.07 (2)	10.00 sd 7.07 (2)	6.00 (1)	9.67 sd 2.52 (3)

Significant differences only	
FD: Oriental and Western	t = 5.06; 7df: 0.01 > P > 0.001

Clinical Presentation

The clinical presentations (mainly with swelling, and/or pain, and as an incidental finding) vary for the FOLs both with regard to the proportions of SR-included reports recording them (Table 8.11-13a) and the proportion of individual cases (Table 11-13b).

Swelling.

Table 8.11a displays no significant difference in proportion of reports considering swelling. Table 8.11b reveals that COFs and FDs present with significantly more cases with swelling than FCODs and FocCODs. This finding is consistent with the non-expansile nature of the CODs. They occur within the medullary bone and tend not to expand the cortices, or, if they do, at least not appreciably. Although both FD and COF cause expansion, they differ in their patterns of expansion, COF, a true benign neoplasm, would be noticed even although its dimensions are likely to smaller than FDs when first diagnosed, because it enlarges a smaller part of the affected bone, which is both clinically and radiologically well-defined whereas FD causes a gradual expansion of the affected bone, in many cases affecting the whole hemi-mandible or hemi-maxilla before being discovered; compare Figures 2 and 3. This may also explain why proportionally fewer SR-included FD reports record the sextant, in comparison to the other FOLs (Table 8.10a). Although this comment is made in the absence of objective volumetric measurements, even if it were available it would still have to

take account of the lesion's site and shape. A localised sphere-like expansion is more likely to be noticed at an earlier stage than a more voluminous, but more generalised and diffuse expansion. Either shape would be earlier detected if they occurred where the overlying soft-tissue was not thick, such as the chin and in the proximity of the malar bone. Lesions invested by thick soft-tissue such as in the posterior mandible are more likely to be detected later when they have become larger.

Table 8.11. Swelling

a. Reports

SWELLING Yes:No	FCOD 10:10	FocCOD 5:5	COF 9:18	FD 12:19
FCOD 10:10		0.00	1.19	0.66
FocCOD 5:5	0.00		0.84	0.35
COF 9:18	1.19	0.84		0.19
FD 12:19	0.66	0.35	0.19	

b. Cases

SWELLING Yes:No	FCOD 33:92	FocCOD 111:328	COF 80:67	FD 167:15
FCOD 33:92		0.06	21.82	139.09
FocCOD 111:328	0.06		42.59	195.00
COF 80:67	21.82	42.59		60.74
FD 167:15	139.09	195.00	60.74	

Pain

There is no significant difference in Table 8.12a with regard to the proportion of reports, which considered pain as a presenting symptom. Table 8.12b displayed FCOD as being significantly more frequently discovered by pain on first presentation than FocCOD, COF and FD. Pain is significantly more associated with FcoCOD than COF; this feature may contribute to distinguishing between them.

Table 8.12. Pain

a. Reports

PAIN Yes:No	FCOD 8:12	FocCOD 5:5	COF 8:19	FD 12:19
FCOD 8:12		0.06	0.56	0.01
FocCOD 5:5	0.06		1.36	0.44
COF 8:19	0.56	1.36		0.52
FD 12:19	0.01	0.44	0.52	

b. Cases

PAIN Yes:No	FCOD 45:68	FocCOD 121:318	COF 17:122	FD 34:148
FCOD 45:68		6.40	27.99	17.59
FocCOD 121:318	6.40		11.35	5.38
COF 17:122	27.99	11.35		2.47
FD 34:148	17.59	5.38	2.47	

Incidental Finding

The proportion of reports recording incidental findings was not significantly higher for FCOD and FocCOD than for COF and FD (Table 8.13a.). FocCOD cases (Table 8.13b) are significantly more frequently discovered incidentally to investigations of unrelated lesions than any other FOL. FD cases are significantly least frequently discovered as an incidental finding.

Table 8.13. Incidental Finding

a. Reports

INCIDENTAL Yes:No	FCOD 10:10	FocCOD 5:5	COF 8:19	FD 12:19
FCOD 10:10		0.00	2.12	0.66
FocCOD 5:5	0.00		1.36	0.44
COF 8:19	2.12	1.36		0.52
FD 12:19	0.66	0.44	0.52	

b. Cases

INCIDENTAL Yes:No	FCOD 52:73	FocCOD 284:155	COF 42:89	FD 4:178
FCOD 52:73		21.45	2.50	82.88
FocCOD 284:155	21.45		43.81	202.03
COF 42:89	2.50	43.81		54.50
FD 4:178	82.88	202.03	54.50	

Clinical presentation, in summary, varies not only with the particular FOL; swelling is most frequently associated with FD, pain with FCOD, and FocCOD as an incidental finding. The incidental discovery scenario reflects the insidious development of COD (no bucco-lingual expansion, no root resorption or displacement), which is consistent with a dysplastic process. This may change only when one or more COD lesions become secondarily infected; this was clearly displayed by the significant age difference between those FCOD derived from a histopathology file and those from a radiology file. Because FocCOD by definition has only one or a few lesions, the chance of it becoming infected is therefore less; hence its more frequent discovery is incident to an investigation for another lesion.

Follow-up and Recurrence

Follow-up and recurrence generally are interrelated. Lesions known to recur (COF if inadequately removed and FD after 'shaving') or progress to more serious lesions (FD undergoing sarcomatous transformation) prompt frequent review (follow-up) to permit early detection and treatment. It is clear that this does not happen for either COD form in Table 8.14a; there is not a single SR-included report for either. Table 8.14b indicates that there is no significant difference in recurrence between cases of FD and COF; the recurrence rate is 8% and 6% respectively for FD and COF. Nevertheless, COF patients are significantly more likely to discharge themselves than those with FD. ($X^2 = 4.36$; 1df; $0.05 > P > 0.01$)

Table 8.14. Follow-up & Recurrence

a. Reports

FOLLOW-UP Yes:No	FCOD 0:20	FocCOD 0:10	COF 8:19	FD 8:23
FCOD 0:20		0.00	7.13	6.00
FocCOD 0:10	0.00		3.88	3.33
COF 8:19	7.13	3.88		0.13
FD 8:23	6.00	3.33	0.13	

b. Cases

RECURRENCE Yes:No	FCOD N/A	FocCOD N/A	COF 12:187	FD 19:252
FCOD N/A				
FocCOD N/A				
COF 12:187				0.09
FD 19:252			0.09	

Radiology

The radiographic appearance of FOLs is central to diagnosis certainly with regards to FD and COF. The FCOD's multiple radiopaque (with or without radiolucent peripheries) lesions on the radiograph are diagnostic for FCOD.

Unfortunately, solitary or localised FocCODs have not been particularly well served by radiology. This is in part due to the varying approaches taken by the reporter attempting to characterise it. This variation reflects the main problem that there is unlikely to be a single feature sufficient to identify all cases. Nevertheless, in addition to marginal definition, there are two other features, which may assist the clinician to formulate a differential diagnosis and management; they are radiolucency and root resorption. Although there are no significant differences between the SR-included reports for any FOL (Table 8.15a.), cases of both FocCOD and COF present significantly more frequently than FD as radiolucencies (Table 8.15b). The difference between FocCOD and COF is not significant. Only about 10% of the COF radiolucencies are multilocular, whereas 6% of FD radiolucencies are; there is no significant difference between them ($X^2 = 0.04$; 1df; $P > 0.05$).

Table 8.15. Radiolucencies

a. Reports

RADIOLUCENCY Yes:No	FCOD N/A	FocCOD 5:5	COF 11:16	FD 11:20
FCOD N/A				
FocCOD 5:5			0.26	0.67
COF 11:16		0.26		0.18
FD 11:20		0.67	0.18	

b. Cases

RADIOLUCENCY Yes:No	FCOD N/A	FocCOD 105:232	COF 55:146	FD 13:256
FCOD N/A				
FocCOD 105:232			0.87	66.17
COF 55:232		0.87		47.49
FD 13:256		66.17	47.49	

In Table 8.16, the Western FocCOD group displays a significantly higher mean number of cases exhibiting a predominant radiological presentation than the Oriental group. This may reflect the greater propensity for Black-Americans for these lesions.

In Table 8.17a cases of COF are significantly more likely to display root resorption than FD or FocCOD (Table 8.17b). The unusual presentation of the root in Figure 3 could represent abnormal root development than true root resorption, which is clearly displayed in Figure 2.

Although COFs displayed significantly more radiolucencies than FD, there are no significant difference with regard to cortication ($X^2 = 0.58$; 1df; $P > 0.05$) bucco-lingual expansion ($X^2 = 0.22$; 1df; $P > 0.05$) and displacement of the lower border of the mandible ($X^2 = 0.00$; 1df; $P < 0.001$), and antral involvement ($X^2 = 0.01$; 1df; $P > 0.05$).

Table 8.16. Mean number of cases displaying a 'predominant radiological presentation'

	All (Number of reports)	Oriental (Number of reports)	African (Number of reports)	Latin American (Number of reports)	Western (Number of reports)
FocCOD	79.50 sd 62.40 (4)	28.50 sd 31.82 (2)	N/A	N/A	130.50 sd 16.26 (2)
COF	16.64 sd 14.62 (11)	10.50 sd 6.36 (2)	13.67 sd 10.70 (3)	N/A	20.17 sd 18.39 (6)
FD	23.00 sd 32.44 (11)	46.50 sd 47.40 (4)	8.33 sd 5.77 (3)	N/A	10.50 sd 8.89 (4)

Significant differences only	
FocCOD: Oriental and Western	t = 8.38: 2df: 0.05 > P > 0.01

Root resorption

Although there are proportionally fewer reports (Table 8.17a), which consider root resorption, COF displays this significantly most frequently in comparison to FocCOD and FD. (Table 8.17b)

Table 8.17. Root Resorption

a. Reports

ROOT RESORPTION Yes:No	FCOD N/A	FocCOD 2:8	COF 5:22	FD 4:22
FCOD N/A				
FocCOD 2:8			0.03	0.27
COF 5:22		0.03		0.40
FD 4:22		0.27	0.40	

b. Cases

ROOT RESORPTION Yes:No	FCOD N/A	FocCOD 0:148	COF 24:83	FD 2:131
FCOD N/A				
FocCOD 0:148			36.48	2.01
COF 24:83		36.48		26.85
FD 2:131		2.01	26.85	

Concluding remarks

Each lesion is different and how it is perceived will depend upon the culture of the community it presents in. A lesion more associated with pain and/ or rapid growth, particularly affecting a child, is more likely to present earlier. While it could be expected that lesions sited more anteriorly particularly in the maxilla, would present earlier, this may not necessarily be the case as reported in an SR on odontogenic myxomas (MacDonald-Jankowski, 2002). In the still traditional working class Hong Kong Chinese patriarchal family, although this is changing, the lower ranked members of the family, in general females, with an apparent lesion may not be sent for treatment if it clashes with the family's other financial priorities (Leung, 1996). The availability of free or moderately priced Western-style treatment may not be an inducer to seeking treatment. The Hong Kong Chinese increasingly subscribe to 'traditional Chinese medicine'- similar although different scenarios may operate within other communities, such as native healers in Africa. The lesions, which are reported after years of prior awareness, may have also been in the meanwhile ineffectively treated by informal or traditional practitioners, which may influence the lesions' eventual presentation to the formally trained practitioner. Some cases, particularly in the present FD study, the ameloblastoma (MacDonald-Jankowski, 2004c and d) and the odontogenic myxoma (MacDonald-Jankowski, 2002) in the same community, feature also the acquisition of substantial dimensions prior to presentation due to a sudden increase in growth or onset of pain. Philipsen and co-authors (2005) remarked upon the non-specific clinical features of most odontogenic neoplasms, "they show slow expansive growth with no or slight pain. In

contrast pain is the most common symptom followed by rapidly developing swelling in nearly all malignant odontogenic tumours." Therefore, a rapid onset of swelling or pain appears instinctively to induce the patient to seek treatment.

The pattern of expansion for FD is more insidious in comparison to the very expansile ameloblastoma or COF, therefore by the time FD does induce a presentation for treatment the lesion will already be extensive and readily diagnosed by clinical examination and radiology; this is most likely to have happened in the present study. In comparison to the other lesions particularly the ameloblastoma, odontogenic myxoma and COF which all require complete ablation, the treatment required for FD is reassurance and some cosmetic reduction if necessary. Investigation for other lesions in the skeleton other than the clinically obvious is unlikely to be exhaustive; the testing for a raised ESR (Jacobsson et al., 1975) is unlikely to be performed, as is the taking of a gynaecological and obstetric history in most dental clinical contexts. The last is also completely absent for those lesions most associated with women, the FCOD.

Chapter 9.

Discussion: GENERAL DISCUSSION

Systematic review

Clearly any SR must by necessity always be incomplete in some regards, because of the restrains imposed by time and resources. Although the present study was almost wholly confined to PubMed, this is the best database for this kind of report. Embase substantially cross-references with PubMed, but is focused more on pharmacological trials. Web of Science truly covers science at its broadest, but shares it 6,000 journal database with far fewer biomedical journals than PubMed. In addition to PubMed central journals were hand-searched and reference lists of identified reports were reviewed. Furthermore, in order to address the paucity of SR-included reports from Latin-America, a second database, LILACS, was searched.

Indices and databases do not record all relevant publications; Medline only indexed 25% of all medical publications that could be described as journals (Egger et al., 1997). Furthermore, according to Greenhalgh (1997b) 50% of the reports indexed in Medline have been misclassified. Therefore, it is essential to follow-up the references in the literature identified by the indices and databases (Rosenfeld, 1996) and carry out a detailed hand-search of journals (Sackett and Rosenberg, 1995). Exclusion of unpublished data from the search avoided the risk of inclusion of covert duplicate publications into the systemic review (Tramer et al., 1997)

Inclusion and exclusion

Although the SRs focused on those FOLs affecting the jaws, admission of some extragnathic cases, particularly in FD, was considered acceptable because it is likely that many FD reports would include some, particularly those affecting the malar bone or floor of the orbit, which is partly made up of by the maxillary bone, which may be viewed in its entirety as the upper-jaw equivalent to the mandible. Admission of such cases should not exceed 10% at the most. The prudence in this decision is clearly displayed by the almost wholly extragnathic report by Boysen and co-authors (1979); they reported 2 cases of proptosis, whereas not one case of proptosis was reported by those reports included in the SR.

In order to ensure inclusion of as many otherwise legitimate reports some leeway was introduced to take account of those few cases that appeared to be COFs or FDs due to other criteria. Almost all reports used a subjective assessment of marginal definition except for that by Slootweg and Muller (1990), and the present COF and FD reports. Re-evaluation of those COFs (MacDonald-Jankowski; 1998) found poorly-defined in 1998, after application of Slootweg and Muller's objective criterion were found to be well-defined. The limit on the number of such cases was set at 10%. The reasons for the exclusion of Su and co-authors (1997a and b) report have already been addressed. Furthermore, the degree of margin definition although crucial for determining whether a FOL is either FD or COF, is as already seen, largely irrelevant for CODs. FCODs are diagnosed by the presence of multiple non-expansive lesions ranging from radiolucency to complete radiopacity. Unfortunately,

there is no suitable radiological criterion to distinguish between FocCODs and COFs other than COF displays significantly more root resorption than FocCODs. As the present study illustrates, root resorption may not be a reliable feature of COF in all communities.

Non-English Languages

A major feature of this collection of SRs is the influence that the inclusion of non-English languages has played. Although more foreign dental journals are being published in English (for example the Italian journal *Minerva Stomatologia* and many Japanese journals, particularly those listed on Index Medicus) many more retain their national languages. Furthermore, journals already converted to English are unlikely to translate past issues in non-English languages. Therefore, language barriers remain. Although it is still possible to perform an influential SR without including non-English journals this is generally restricted to reports on new technologies, such as osseointegrated implants, such as that published by Bryant, MacDonald-Jankowski and Kim (2007) and commissioned by the Academy of Osseointegration. This particular SR was further subjected to scrutiny by an international team of experts, many of them major authors in the field of implantology to ensure that all relevant reports have been included. It had been decided by the Academy that only English papers would be included, because although there would undoubtedly be reports in the non-English literature, they would be unlikely to influence the outcome of the SR. Even without inclusion of non-English reports, this was already a huge and expensive undertaking, which

identified 3200 reports for further consideration. Unfortunately, when dealing with pathology one must consider its global dimension in order to fully characterise a particular lesion. Such a SR must be open to the global literature in order to ensure that as many communities are represented in the final SR. Table 8.1 clearly indicates that foreign language reports contributed to 25% on average to each of the 7 SRs on lesions affecting the jaws

Although, Table 8.1 displays only those reports included, many more non-English language papers were read but not included, and many of those have been identified in the individual SRs.

The role of radiology

The respective roles of radiology and histopathology

Their roles differ with perspective, whether they are viewed retrospectively or prospectively. The retrospective approach is best demonstrated in most textbooks, including White and Pharoah (2004), beginning with the definitive diagnosis, whereas in the prospective view of the clinician the definitive diagnosis marks the end of the diagnostic process

Retrospective view.

Although the current role of histopathology is simply to determine whether or not the lesion is a FOL, it is of the utmost importance, because failure of a prospective FOL at this point, excludes it from further consideration. After this confirmation that the lesion is an FOL, the central defining radiological criterion was the degree of marginal definition, which was crucial to determine COFs from FDs. If FD and COF were the only FOLs then it would have been easy, but there is a third broad group, the COD, which is subdivided into FCOD and FocCOD. Radiologically the former's multiple lesions within the alveolus readily identify it, but such cannot be said for the FocCOD. The FocCOD, recently characterised albeit incompletely, is becoming widely recognised as a clinical entity; the WHO's 2005 edition of the classification of head and neck neoplasms (Slootweg, 2005) has now recognised it. Nevertheless, with the passage of time we should expect developments in this area. It is clearly a catch-all category for lesions that do not fit in with the other FOLs. Its clinical and radiological presentations are variable, and its histopathology non-specific other than it is a FOL, leaves very little scope to diagnose it as a defined lesion in its own right. According to the retrospective approach this is not a problem, because the FocCOD has formalised the diagnostic 'dustbin' into which hitherto nonconforming FOLs were tossed.

The Prospective view.

The patient presents him/herself for treatment for pain or swelling (arising from the as of yet undiagnosed FOL), or the symptomfree and hitherto undetected FOL is detected incidentally to the investigation of an unrelated clinical problem.

These incidental findings can arise from the clinical or the radiological examinations. From the clinical and radiological features, the clinician will consider the differential diagnosis. [The differential diagnosis of FOLs will be addressed later]. Many FOLs will be diagnosed at this stage and often nothing prescribed other than reassurance and periodic review. For other lesions referral and biopsy may be required. Eventually, the histopathology of a small number of these lesions will be analysed and a definitive diagnosis generated. The lesion, if not already, will be treated in manner appropriate to the definitive diagnosis. Nevertheless, pathologists have continued to develop more laboratory tests with the aim of understanding these lesions, namely FD and COF, better. So far they have produced mixed results and do not take us far beyond where we have been for nearly the last 2 and a half decades, based on the degree of definition of the radiological apparent margin of a lesion, which is histopathologically a FOL. This has already been fully discussed in the FD SR. This thesis has revealed more clinical and radiological features that could be used as a launch pad to understanding these lesions' progression. The present author's endeavours have been hampered both by a lack of detail in many of the reports and a lack of longer-term follow-up.

The four global groups

Dividing the SR-included reports into 4 global groups on the basis of the predominant genetic subgroup of humanity allows some comparison to be made between them. This is already being done; patients of Sub-Saharan African origin frequently are tested for sickle-cell disease prior to procedures undertaken under

general anaesthetic. This division is necessarily an approximation because not only have populations migrated, but also over the last few centuries this migration has been substantial resulting in significant intermarriage between these subgroups. Nevertheless, the distribution of the reports indicates that there is substantial disparity between these groups. Other than Americans, the Africans (particularly the Nigerians) and the Orientals (particularly the Japanese) display a professional interest in producing such reports; those of Latin-America appear less inclined. This may reflect in part a tendency for Latin-American reporters to use Schajowicz' (1993) classification of (extragnathic) bone neoplasms rather than either edition of the classification of odontogenic neoplasms (Pindborg et al., 1971; Kramer et al., 1992) thus leading to their frequent exclusion.

The importance of Conventional Radiography in the diagnosis of FOLs

The radiological modality in this report was confined to conventional radiography, which will remain the principle modality not only because of cost, convenience and lower radiation dose reduction, but also spatial resolution. The high spatial resolution of conventional radiography is essential to determine the precise diagnosis of many FOLs primarily with regards to their degree of marginal definition. MacDonald-Jankowski et al. (2004b) reported that this is less clear for CT. Indeed the best spatial resolution of cone-beam CT is 0.1 voxel size, which is about 5 line pairs per millimetre (lpmm) (MacDonald-Jankowski and Orpe, 2006), which is about the same for a panoramic radiograph or below the 20 lpmm of intra oral film or 11-25 of digital radiography (Farman and Farman, 2005). Therefore,

although Reichert and co-authors (2005) have advised more cross-sectional images, these should compliment rather than replace conventional radiography.

Earlier reports using earlier panoramic technology (with only 2 or 3 centres of rotation, lower peak kilovoltages and slower intensifying screen-film systems) reported artefacts unlikely to be observed in images created by modern units. These would contributed to the phenomenon Waldron and Giansanti (1973) reported. They reported that the anterior aspect of their FDs were 'well-defined' on the panoramic radiograph, which was not confirmed either by surgery or occlusal radiograph.

Technology with regards to conventional radiography continues to advance; digital radiography has become well established in dentistry but brings its own challenges. Hitherto, the clinician under optimal viewing conditions (bright viewing box/illuminator in reduced ambient lighting) has placed justified confidence in an optimally developed film, which regardless of film-speed had spatial resolutions in excess of 20 lpmm. This is no longer the case. As Farman and Farman (2005) have revealed, the spatial resolution varies widely between digital systems and models. Furthermore, both the spatial resolution and bit depth of the monitors will have their effects. Ideally, the monitor should display a pixel-to-pixel correlation and an adequate range of grey-levels (12 bit-depth). Furthermore, brightness of the monitor, human-contrast sensitivity and its calibration become issues, as these affect the ability to detect high-spatial-resolution and low-contrast-resolution features. (MacDonald-Jankowski and Orpe, 2007a and b).

All these technical issues notwithstanding, the SRs (particular those concerning FDs and COFs) had to be based firmly on this widely accepted radiological criterion of marginal definition. Although this may not apply to every true case of FD or COF so far it has served oral and maxillofacial practitioners very well. Su and co-authors (1997a and b) were right to consider the possibility of other features which may also assist differentiating between COD and COF, but erred by not first identifying the COFs according to classically well-defined margins and correlating these lesions with their other features. Once these had been statistically confirmed then these other features could be applied to the poorly-defined cases suspected of being COFs.

Technically, this should be relatively easy to perform; all that is required is a large histopathological file supported by comprehensive clinical reports and radiographs. But even if this were the case, increasingly oral pathology services are being annexed by medical pathology services with their own filing systems based on a different WHO international classification of bone tumours (the second edition by Schajowicz, 1993). This classification has been used by a number of reports (excluded from the present SRs) with regards to FD. Although the summary definitions between Pindborg and co-authors (1971) and Schajowicz (1993) are broadly similar, only the former emphases the poorly-defined margin of FD of the jaws, whereas the latter concentrates on the ground glass appearance and the presence of cartilage; the latter does not appear in gnathic FD. Furthermore, COF and CODs are fully recognized as separate lesions by Pindborg and co-authors (1971), whereas only OF renamed 'osteofibroma' is recognized (Schajowicz, 1993). It is

clear from at least one report (Zhou et al., 1989) that an attempt to make use both WHO classifications resulted in the exclusion of a number cases described as 'osteofibromas'.

Interestingly, as mentioned in the introduction, the WHO's 2005 classification supervised by Reichart and Philipsen (2005) have recently advanced the use of 'ossifying' fibroma (Slootweg and El Mofty, 2005) rather than COF and 'osseous' dysplasia (Slootweg, 2005) instead of COD. Therefore, for the first time there is the real possibility that all head and neck specialists will use the same WHO authority (the 2005 and subsequent editions) and will be able to communicate with each other with the utmost clarity, particularly with regards to FOLs. The term OF would appear to have been first re-used to replace COF by Brannon and Fowler (2001), then subsequently by Reichart and Philipsen (2004). It is interesting that OF is precisely the term which had been only relatively recently vacated by Schajowicz (1993) in preference for 'osteofibroma'. Will the next stage in FOL nomenclature be that those lesions currently called COFs will eventually be called 'osteofibromas'?

Relative Period Prevalence and 'number of lesions per hospital per year'.

Relative period prevalence (RPP) of an odontogenic tumour is the usual method of comparing one lesion with another in the same study. RPP has 2 main disadvantages. It assumes that all lesions biopsied or surgically treated will have been sent for histopathological evaluation and will be registered.

Furthermore, the taxonomy and classification of lesions change over time as is evident from the 'lumping' and 'splitting' displayed in Figure 1.

The RPP is dependent on the presence and diagnosis of other WHO classified odontogenic lesions and will also be affected by the edition used. COF is a very good example. In the first edition of the WHO classification of odontogenic neoplasms, CF was a benign neoplasm related to the odontogenic apparatus, whereas OF was an osteogenic neoplasm (see Figure 1). Therefore some COFs would have a RPP as an odontogenic neoplasm, but not the others. Over 20 years later both CF and OF were already firmly under the umbrella of COF and osteogenic neoplasms where they remain. They are now completely absent from modern reports of odontogenic neoplasms; such as that by Bucher and co-authors (2006), Olgac and co-authors (2006), Adebayo and co-authors (2005) and Ladeinde and co-authors (2005), whereas they still appear in the less frequently published more-inclusive reports in the 'bone pathology' section of oral and maxillofacial pathology, such as that by Jones and Franklin (2006a and b). Furthermore, this recent report also displays the other phenomenon, namely that experienced pathologists may take a different point of view with regards to classification of a particular lesion; Jones and Franklin (2006a and b), placed CF and OF along with FD in the 'bone pathology' section, but CODs in the 'benign neoplasm' section. After taking account of all of the above, it would appear that RPP has little real applicability for comparing the caseload a particular lesion imposes on a particular community in comparison to another.

The 'number of lesions per hospital per year' is a better indicator of the annual contribution that a lesion could make to the caseload of the hospital or hospitals sited within a particular community. This is important because the predilection of certain lesions is higher for some communities, for example ameloblastoma is higher for Black Africans, Chinese and Japanese than it is for others, particularly in North America and Europe. This predilection may affect the local differential diagnosis and resource-planning.

Philipsen and co-authors (2005) observed that the ameloblastoma is the most frequent of all odontogenic neoplasms in African and Oriental reports, whereas the odontoma is the most frequent neoplasm in North American reports. They suggest one reason for this discrepancy; the source of the reports. In Asia and Africa, the reports come from oral and maxillofacial surgical units in medical hospitals where in North America they come from dental schools and hospitals, where the use of panoramic radiography readily displays the hitherto undetected odontoma, which once removed will be forwarded for a histopathological investigation. In the developing world it is the surgical specimen of the ameloblastoma, which is most likely to be sent for a histopathological investigation for proper diagnosis and appropriate treatment. This reflects what Sawyer (1985) had already observed. Furthermore, he reported that the higher frequency of neoplasms in Africa could reflect the 'harvesting phenomenon' of benign odontogenic neoplasms caused by their characteristic slow-growing non-lethal nature. This may lead to the creation of a reservoir of disease, which a formal oral and maxillofacial service must first

address upon its initial establishment in a particular locale, because this reservoir undoubtedly must mask and distort the real incidence of the lesion.

Of course the numbers of a particular lesion diagnosed may increase over the study period due to increased expertise, accessibility and referral to that hospital, but this would also apply to the RPP. Furthermore, unlike the RPP, the 'number of COFs per hospital per year' will be unaffected by substantial variation of the numbers of other odontogenic tumours.

The present study reveals a marked variation in 'incidence', particularly for COFs. Twenty were diagnosed within the first 10 years of the establishment of PPDH as the first formal oral and maxillofacial teaching and academic facility in Hong Kong; the previous comparable presence was that of the British Armed Forces. In the subsequent 12 years only 4 more were diagnosed at the same facility. Although, undoubtedly, the first 20 represented the untreated reservoir of this lesion, this may not wholly account for the sharp fall in the incidence. A similar phenomenon was reported in a SR of ameloblastomas for a Nigerian community (Kaduna); the 'number of cases' fell from 13.8 in Ajagbe and Daramola's 1960-1983 report (1987) to 5.4 in Aritoba and co-authors' 1980-1994 report (1997). This fall was considered to represent more likely a fall in prevalence occasioned by the reduction of the initial reservoir of untreated ameloblastomas rather than a reduction in annual incidence. It was this initial reporting of newly established formal oral and maxillofacial services outside the Western world which accounted for the increased 'number of ameloblastomas" from the 1990.

In addition to improved diagnosis and appropriate treatment, the establishment of a formal oral and maxillofacial facility may bring one more invaluable advantage, the training of specialists within that community to eventually work within it. Since 1989, the advent of Professor Henk Tideman to the chair of Oral and Maxillofacial Surgery, saw, among others, a substantial increase in specialist oral and maxillofacial surgeons throughout the Hong Kong community. They will have undoubtedly been responsible in part for the general reduction in lesions diagnosed at PPDH. Nevertheless, FD cases displayed a more complex pattern of admission. Several had already had their FDs diagnosed, and on occasion treated elsewhere in Hong Kong. More were already aware of that lesion for years prior to admission. Irrespective of their histories, almost all these lesions were of substantial dimensions upon admission to PPDH.

Although the 'number of lesions per hospital per year' can be equated to be the annual incidence in some reports (based on the number of cases admitted to that particular hospital which was established in an area that hitherto did not have formal medical care) it could very well reflect the reduction of the already existing and untreated reservoir of disease, than the annual incidence experienced in longer established hospitals in areas with long and well-established formal medical care.

Another important factor that is likely to affect the 'number of cases per hospital per year' is the length of time a lesion has been recognised as a distinct entity. The large number of cases both in Su and co-authors 91997) and Summerlin and Tomich's (1994) reports may merely reflect that prior to this, referring clinicians

considered it to be a neoplasm, requiring surgery. This is clearly obvious in Table 5.2 in the present study.

A presumption that the reports will be free of significant error.

There is general but rebuttable presumption, that all peer-reviewed reports will be free of significant error. It is part of the natural human condition to err, and not all errors are fatal to a report's contribution to clinical science. Furthermore, what constitutes a significant error in one area may not in another; for example, a single error in translation can result in the exclusion of a report; the word 'maxilla', and its variants, in Romance languages, meaning 'jaws' was on at least two occasions in the SR on dentigerous cysts mistranslated as 'maxilla', leading to the real risk of the reports being excluded simply because they were perceived as reports of a specific jaw. This would have happened if 'set searching' had been used. In addition Greenhalgh (1997) remarked that 50% of entries in Medline are miscataloged. This and the lack of appropriate MeSH were the main reasons why 'set searching' was not employed and the more laborious hand-searching and reference harvesting preferred.

It was assumed that reported series of cases surveyed represent either a population-based, or a sampling framework of the actual occurrence of the pathoses.

The vast majority of reports were excluded from each of the 4 present SRs not because of perceived errors, but simply because they reported lesions that differed significantly from those desired for inclusion by the SRs. These significant

differences were with regards to differences in histopathology, radiology and failure to report (the likelihood of) the full caseload of those specific lesions experienced by the clinicians in a particular community. It was appreciated that different clinicians would view the same lesion or feature of that lesion slightly differently. Sometimes these small differences, such as the degree of definition of the margin, can have profound effects on the diagnosis, leading either to a FD that needs no treatment or to a COF that requires surgery. Therefore, it is conceivable how one decision could lead to inappropriate treatment for that particular patient and an adverse medico-legal outcome. For such a feature, it is preferred that an objective parameter is used; such as that by Slootweg and Muller. Nevertheless, it has to be accepted that this parameter has not been used, other than by the present author. Therefore, some allowance has to be made such an eventuality, hence the 'less than 10% rule' allowance for Criterion 2. of the COF and FD SRs.

Although application of Slootweg and Muller's (1990) parameter within the present reports on the Hong Kong Chinese has hitherto been informally supported by histopathological, clinical and follow-up findings, a formal testing of such a parameter is required. Unfortunately, the 'gold standard' of histopathology as suggested by Stheeman and co-authors (1995) is of little use except to say that all lesions are FOLs. Additional information must come from clinical behaviour including very long term follow-up. A FOL, which may appear inconclusive at a particular point in time, may later reveal its true identity (Noffke, 1998). Although some FDs can be derived from McCune-Albright Syndrome cases, as discussed earlier, some of the features observed in such cases by Akintoye and co-authors

(2004) may be associated with the particular endocrinology and age, and be of little assistance in the diagnosis of the monostotic cases which give rise to almost all FD/COF diagnostic problems. Petrikowski and co-authors (1995) conducted a comparative study on osteogenic sarcoma, FD and osteomyelitis; three lesions whose histopathological picture may overlap. Unfortunately, some of the chosen cases displayed features (such as spiculations and onion-layer periosteal reactions) that are already widely known not to appear in FD. It would have been better to choose cases that were truly inconclusive, which can then be subject to a checklist of radiological features.

The predilection for females.

The predilections of COF, FCOD and FocCOD for females are significant features of these lesions, particularly the FCOD. In relation to both FCOD and FocCOD, Kawai and co-authors (1999) reported the very few Japanese males affected with these lesions were older than the females. Furthermore, Kawai and co-authors (1999) suggest that CODs represent a dysplastic process related to hormonal imbalance that influences bone remodelling. This effect may not be merely confined to CODs, but also to FD and COF. FD has been reported to undergo increased growth during pregnancy. The present COF study indicates that some lesions may begin growing (again) in perimenopausal women. Unfortunately, this hypothesis remains merely that until clearer evidence is obtained first by full gynaecological histories and hormonal testing of larger groups of patients who have been followed up over a long period.

The Hong Kong Chinese female may display at least one significant dental difference from males from puberty; young females display significantly more taurodontism, particularly in the second molar (MacDonald-Jankowski and Li, 1993b), which is undergoing root formation during puberty. The unusual shaped roots reported in Maxillary Case 3 do not display taurodontism and occur in a male.

Differential diagnosis of FOLs

The majority of lesions that appear prominently in the differential diagnosis of FOLs are radiopacities occurring in the jaw bones; these are idiopathic osteosclerosis (IOS), MacDonald-Jankowski (1999b) condensing osteitis (CO; secondary to dental inflammation; MacDonald-Jankowski, 1999b), and odontomas (MacDonald-Jankowski, 1996b). Once the film-development artefacts, and soft-tissue and metallic (iatrogenic) radiopacities have been excluded then four important aspects of the radiopacities can be considered sequentially as shown on the flow-chart (Figure 5). These are:

1. Are there multiple or single (solitary or focal) radiopacities?
2. Is the radiopacity/s well-defined?
3. Is the radiopacity/s sited above the mandibular canal?
4. Is the radiopacity/s surrounded by a radiolucent space?

Multiple or single lesions suggest differing aetiology, the former a likely systemic cause and the latter a local cause. It can be seen from Figure 5 that all

of the multiple lesions have recognised familial (Gardner's syndrome, 'florid cemento-osseous dysplasia' and 'periapical cemental dysplasia') and perhaps even a genetic tendency (familial gigantiform cementoma).

It is now generally accepted that it is reasonable to use the mandibular canal (inferior dental canal) as an arbitrary limit to the alveolar process or the tooth-bearing part of the jaws, particularly because the teeth develop above it in the foetal jaw and generally retain that relationship. Nevertheless, it should be noted that not only do lesions with a clear odontogenic origin, such as odontomas (MacDonald-Jankowski, 1996b) and cementoblastomas (MacDonald-Jankowski, 1992b), arise within the alveolus, but so do others, such as CODs, IOS and the majority of COFs, which do not appear to have a clear odontogenic origin. As they expand they generally will displace the mandibular canal downwards. Conversely, lesions arising below it may be considered to be non-odontogenic lesions which if sufficiently large may displace the mandibular canal upwards, as demonstrated of FD by Petrikowski and co-authors (1995). The subjective impression that lesions common to the general skeleton appear intrinsically to abhor the alveolus is false, as FD also on occasion displaces the mandibular canal downwards, indicating that it may have initially arisen within the alveolus. A more likely reason is that the alveolus proportionally occupies such a small volume of the jaws with a proportionally smaller chance of general disease arising in it. It is also relatively transient; it can atrophy spectacularly after removal of the teeth (Watt and MacGregor, 1986).

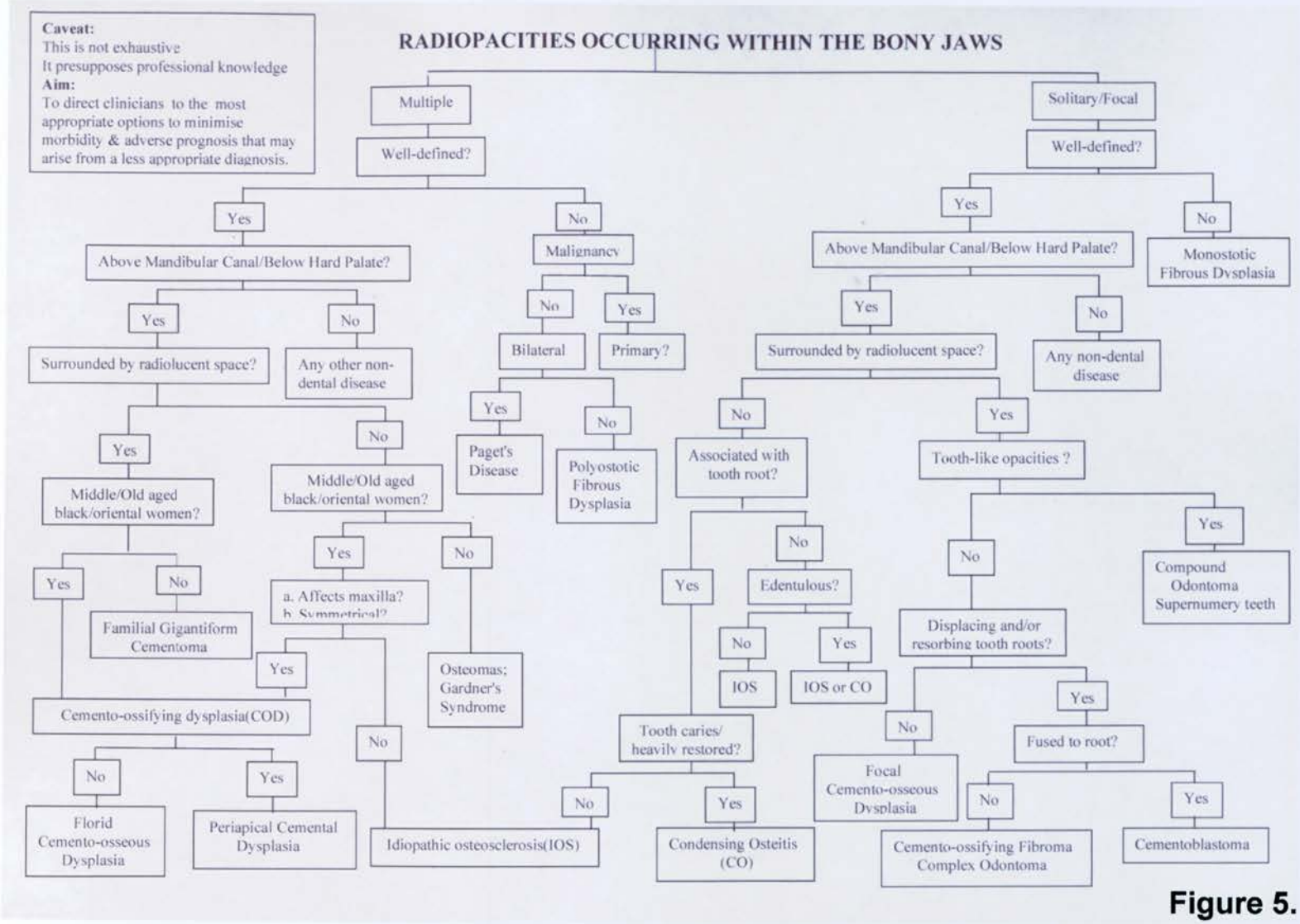

Caveat:
This is not exhaustive
It presupposes professional knowledge
Aim:
To direct clinicians to the most appropriate options to minimise morbidity & adverse prognosis that may arise from a less appropriate diagnosis.
RADIOPACITIES OCCURRING WITHIN THE BONY JAWS
Multiple
Well-defined?
Yes
Above Mandibular Canal/Below Hard Palate?
Yes
Surrounded by radiolucent space?
Yes
Middle/Old aged black/oriental women?
Yes
Familial Gigantiform Cementoma
No
Cemento-ossifying dysplasia(COD)
No
Florid Cemento-osseous Dysplasia
Yes
Periapical Cemental Dysplasia
No
Any other non-dental disease
No
Middle/Old aged black/oriental women?
Yes
a. Affects maxilla?
b. Symmetrical?
Yes
No
Idiopathic osteosclerosis(IOS)
No
Osteomas; Gardner's Syndrome
No
Malignancy
No
Bilateral
Yes
Paget's Disease
No
Polyostotic Fibrous Dysplasia
Yes
Primary?
Solitary/Focal
Well-defined?
Yes
Above Mandibular Canal/Below Hard Palate?
Yes
Surrounded by radiolucent space?
No
Associated with tooth root?
Yes
Tooth caries/ heavily restored?
No
Condensing Osteitis (CO)
No
Edentulous?
No
IOS
Yes
IOS or CO
Yes
Tooth-like opacities ?
No
Displacing and/or resorbing tooth roots?
No
Focal Cemento-osseous Dysplasia
Yes
Fused to root?
No
Cemento-ossifying Fibroma Complex Odontoma
Yes
Cementoblastoma
Yes
Compound Odontoma Supernumery teeth
No
Any non-dental disease
No
Monostotic Fibrous Dysplasia

Figure 5.

Fig. 5

The maxilla does not have such a well-defined arbitrary limit for the alveolar process, because the superior alveolar (dental) nerve, the maxilla's equivalent of the mandibular nerve, is not radiologically apparent.

Nevertheless, an arbitrary margin for the superior margin is fairly easy to define. Radiographically, on both panoramic radiographs and lateral cephalograms the alveolar process is below the image of the hard palate. Any radiopacity confined to the alveolar process below the hard palate may be considered to be those lesions already mentioned with regards to the mandibular alveolus. Although the boundary between the maxillary antrum and the alveolus is very variable, with the antrum frequently pneumatising the alveolus especially in the premolar region, the antrum's response to disease can assist the radiologist. Its obliteration by odontogenic tumours and FD differentiates them from Paget's disease, which generally spares the antral lumen. Wang and co-workers (2005), in addition to their own 2 cases reported no more than 7 other published reports of Paget's affecting the jaws thus suggesting that Paget's disease is very rare in the Chinese. Although according to H'ng and Ho (2005) this is due to under-reporting Paget's in this community; nevertheless, its incidence is still very low. Benign neoplasms and odontogenic cysts displace upwardly the antral floor to create a rounded expansion when seen on panoramic radiographs and lateral views. Their radiodensity readily allows their differentiation from lesions arising within the antral mucosa, such as the antral mucosal cyst (MAC), which are obvious only by being silhouetted against the air-filled antral lumen (MacDonald-Jankowski, 1993 and 1994). It is also important to appreciate that cystic lesions arising

from odontogenic tissue, such as keratocysts, dentigerous cysts and unicystic ameloblastomas, can also similarly appear as radiopacities in the antrum, but, unless secondarily infected, can be distinguished from the MAC by having a radiopaque periphery representing the upwardly displaced floor of the antrum; see MacDonald-Jankowski's figures for odontogenic keratocysts (MacDonald-Jankowski, 1992b). Also unlike lesions arising within the alveolus the floor of the antrum below a MAC appears as an intact and undisplaced cortex.

Of course flow-charts cannot fully provide for all rare exceptions without becoming unduly cumbersome. Rare lesions such as multiple COFs are only occasionally reported in the literature, a testimony to their rarity. 'Any other non-dental disease' refers to those radiopacities generating diseases found in the rest of the skeleton such as sclerosing osteomyelitis, osteoid osteitis and osteoblastoma in the differential diagnosis of solitary/focal radiopacities, and metastasis from carcinoma of the breast, thyroid and prostrate in that of multiple radiopacities.

The differential diagnosis generally ranks the lesions in order of their relative prevalence, taking account of the patient's age, sex, race, country of origin and anatomical location of the disease. In the jaws 90% of CODs occur in women, predominantly Black or Oriental patient, over 30 years of age. Site predilection of FD is for the maxilla (MacDonald-Jankowski, 1999a), whereas that for cementoblastoma (MacDonald-Jankowski, 1992b) is the first molar and

premolar (MacDonald-Jankowski, 1999b) and that for the PCOD is the mandibular incisors (Pindborg et al., 1971).

FCOD is usually limited to the alveolar process, whereas chronic diffuse sclerosing osteomyelitis is usually a single lesion limited to the body of the mandible on one side extending from the alveolus to the lower border and occasionally into the ramus (Groot et al., 1996).

The odontoma is actually a hamartoma (MacDonald-Jankowski,1996b). The complex form of this lesion can display all the radiologic features of COF. Although the majority of odontomas do not exceed the dimensions of normal teeth, a number of very large odontomas, especially the complex form, have been reported (MacDonald-Jankowski, 1996b).

A further radiopaque lesion that appears with even greater frequency is IOS (MacDonald-Jankowski, 1999b). It is important to recognise this generally conspicuous well-defined radiopacity because it merits no treatment. It can be distinguished from COFs and odontomas because it has no radiolucent periphery and even if large causes no expansion (MacDonald-Jankowski, 1999b). The main difference between IOS and condensing osteitis (CO) is that the latter is directly associated with a carious or heavily restored tooth and is indicative of pulpal necrosis, whereas IOS may be associated with a non carious or restored tooth or be completely unassociated with teeth, while still remaining within the alveolus. The radiodensity and size of IOS as with most

other radiopacities observed can vary markedly. Furthermore, an IOS can be indistinguishable from a late stage COD presenting as a complete radiopacity.

All FOLs, CODs and COFs in particular, have a well-defined radiolucent initial stage, which could simulate lesions that present classically as radiolucencies. Therefore, it should be appreciated that most classically radiopaque lesions are radiolucent in their earliest stages and could appear in the differential diagnoses of significant radiolucent lesions such as ameloblastomas (Sakato, 1977b), odontogenic keratocysts and myxomas. Anand and co-workers (1967) were concerned that a radiolucent COF may be mistaken for an ameloblastoma. One COF in the present study (Table 6.3) was considered to be an ameloblastoma. Three solid ameloblastomas in the same community included COF in their differential diagnosis. (MacDonald-Jankowski et al., 2004d).

Paucity of serious outcomes in SR-included reports on FOLs.

A surprising result of the SRs was the paucity of serious outcomes of malignant change for FDs, local destruction caused by COFs, and threat to vision by both. Although the literature reports many such cases, they clearly do not occur within the context of consecutive case series included in the present SRs. Therefore; out of a synthesis of 788 SR-included FDs not one was reported as having undergone malignant change. This could suggest that such an event is rare. Only one report (Daramola et al., 1976), excluded under 'Criterion 2', reported a case occurring during the period of their study. With regards to sarcomatous transformation, many

reports did not follow their cases for long enough. Nevertheless, virtually no SR-included report reported destructive lesions either on presentation or on follow-up.

The lack of threat to vision may be explained by the fact that almost every SR-included lesion primarily affected the jaws. Although it is clear from MacDonald-Jankowski and co-authors (2004b) report on the CT presentation of FDs, almost all included in the present study, that many such lesions did obdurate the maxillary antrum and reach the orbital floor, they caused little orbital disturbance, perhaps because they were still distant from the optic nerve.

All together this would suggest that in FOLs confined primarily to the jaws, serious outcomes are not common. This of course does not mean that FOLs and their sequalae minimally impact the patient and his/her treatment, as already discussed, longer term follow-up is required of all FOLs, even the FocCODs.

What is the continuing role of biopsy in FOLs?

The effect of biopsies on FOLs is unreported. Do they as other surgical procedures, induce complications? Although the effect that an absence of biopsy has on diagnosis and management is also unknown, its effect on the report is very clear. Chomette and co-authors' (1987) report was excluded because only two-thirds of their cases were accompanied by histopathological confirmation. The reports by Melrose and co-authors (1976) and MacDonald-Jankowski (1992) were included in

the FCOD SR only with radiology findings. Biopsy is not necessary to identify lesions already definitively diagnosed on clinical and radiological findings.

Concluding remarks.

Although a technical challenge for the surgeon, diagnosis of a large FOL is unlikely to challenge the specialist radiologist's or dental surgeon's diagnostic acumen as is clear in a recent report on FD (MacDonald-Jankowski, 1999a). Difficulty is more likely to arise with smaller lesions. Also Waldron and Giansanti (1973) mistook 4 lesions with poorly-defined peripheries as COFs. For example a radiolucent lesion in an infant was diagnosed as a FD only to be diagnosed later as a JOF (Noffke, 1998). In another case a lesion labelled as an 'atypical FOL' was subsequently found to be a low-grade osteogenic sarcoma (Koury et al., 1995).

A complex genetic relationship may exist within this whole class of lesions; Cangers and co-authors (2004) reported COFs in a father and daughter. This was already discussed with regards to FD earlier (Bianco and co-authors, 1998). In addition to genetics, immunohistochemistry (Granado et al., 2006; Pimenta et al., 2000) and) has also been applied to FOLs revealing some more details. Nevertheless, neither has yet reached a level that can profoundly affect diagnosis and treatment planning; this is likely to be achieved with the fullness of time.

The major problems encountered by the authors of WHO's second edition was not only the complexity of the tissues involved but also the rarity of some

lesions which made it difficult to accumulate a large number for study and comparison (Kramer et al., 1992). Although the principles of SR have been applied to FD, the difficulty of this task has been aggravated by insufficient detail in the literature, particularly of radiological features (MacDonald-Jankowski, 1999a). A further difficulty is that, with the exception of a few long-term follow-up case reports, there are no reports of really long-term follow-up series of any FOL in particular those, on current evidence, which do not indicate routine surgery, such as FD and CODs

The purpose of a clinical classification should be more than mere taxonomy; it should assist the clinician of the day to achieve a diagnosis that may be transformed into an appropriate treatment plan. With regards to COD, this may mean doing nothing, simply because no treatment is generally appropriate. Almost all COFs should be treated surgically, whereas FD cases are treated according to their clinical presentation, ranging from review and follow-up to surgery necessary to save the patient's sight or reduce grotesque deformity.

Although the present classification has appeared to serve us well for the moment the deviant behaviour or presentation of a minority of lesions suggests that our understanding of these lesions is incomplete. Of these reports are those such as Iida's (2006) reports of multiple CODs arising from impacted teeth associated with odontogenic lesions> This adds some weight to the undoubted association particularly of CODs with the alveolus, suggests some odontogenic influence. Only

further study with long-term follow-up of cases will confirm or refute this and other impressions.

This study began on the premise that radiology had a central role in the diagnosis of FOLs affecting the jaws, with particular regard to marginal definition. Although the reviews of the literature and a case sequence reinforced this premise, it was somewhat disappointing that the great majority of reports contained little radiology. This is crucial because the diagnostic dilemma for gnathic FOLs now exists between COFs and FocCODs. This is not merely so that once again the clinician can be sure whether the lesion before him/her requires (COF) or does not require (FD or FocCOD) surgical ablation. FocCOD unlike FDs would appear to be common particularly in Black African and Oriental patients. Their presence in those edentulous ridges to be restored to optimal function by osseointegrated implants, challenges the modern clinician. The challenges are: Are they definitely FocCODs? If removed - do they heal well enough to allow successful placement and retention of osseointegrated implants?

Further study of FOLs in this Hong Kong Chinese community should examine the effects of hormonal changes and use of TCM, fluoridation of the water supply on FOL lesions. This would require the taking of gynaecological, obstetric and alternative medicines histories.

Most published clinical reports include diagnosis and treatment and perhaps follow-up for a few years. Unless the disease is completely ablated, life-long follow-

up may be necessary, particularly for FD which may be a life-long chronic disease (Posnick, 1998) and not merely a hamartoma that burns-out soon after puberty. Follow-up is not a casual undertaking for the patient, at each visit the patient must adjust his/her life, take time off from work, in addition to being reminded that s/he has a disease. Both COF and FD have similar recurrence rates but patients discharged themselves more significantly from the COF follow-up, perhaps the awareness that they still possessed disease encouraged those patients with FD to continue with the follow-up of their disease.

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Appendix

CORE PUBLICATIONS ON FIBRO-OSSEOUS LESIONS

MacDonald-Jankowski DS. (1992) Gigantiform cementoma occurring in two populations, London and Hong Kong. Clin Radiol.;45:316-8.

MacDonald-Jankowski DS. (1996) Florid osseous dysplasia in Hong Kong Chinese. Dentomaxillofac Radiol.;25:39-41.

MacDonald-Jankowski DS. (1998) Cemento-ossifying fibromas in the jaws of Hong Kong Chinese. Dentomaxillofac Radiol.;27:298-304.

MacDonald-Jankowski D. (1999) Fibrous dysplasia in the jaws of a Hong-Kong population: radiographic presentation and systematic review. Dentomaxillofac Radiol.;28:195-202.

MacDonald-Jankowski DS. (2003) Florid cemento-osseous dysplasia: a systematic review. Dentomaxillofac Radiol.;32:141-9.

MacDonald-Jankowski DS. (2004) Fibro-osseous lesions of the face and jaws. Clin Radiol. Jan;59(1):11-25. (This was the 3rd most frequently downloaded article for *Clinical Radiology* for 2003/2004: *Clinical Radiology* 2005: 60: 139-140.) (It was also the 3rd most downloaded for 2005; ScienceDirect (http://top25.sciencedirect.com/index.php?subject_area_id=17&journal_id=00099260).

Clinical Radiology (1992) **45**, 316–318

Gigantiform Cementoma Occurring in Two Populations, London and Hong Kong

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The gigantiform cementoma presents as multiple opacities in the tooth-bearing areas of the jaws. Sixteen cases are presented, six of British Negresses and 10 of Hong Kong Chinese females. The differential diagnosis and management are briefly reviewed. MacDonald-Jankowski, D.S. (1992). *Clinical Radiology* **45**, 316–318. Gigantiform Cementoma Occurring in Two Populations, London and Hong Kong

The gigantiform cementoma is an uncommon lesion that is usually observed as an incidental finding on the dental panoramic radiograph. It presents classically as radiopacities especially affecting the molar-premolar region of all four dental quadrants. Although it is innocent, occasionally requiring treatment for the pain and swelling associated with a secondary infection, it is clinically important as it may mimic other lesions.

Cementum is normally deposited on the roots of teeth continuously throughout life to compensate for the loss of tooth height due to the normal wear that accompanies the grinding and chewing of food. The term hypercementosis is employed empirically when the layer of cementum laid down is excessive. The stimuli are infection, abnormal function and Paget's disease. A cementoma is a circumscribed tumour-like mass of cementum sited at the apex of a tooth (Lucas, 1984).

The cementoma belongs to a group of diseases called fibro-osseous lesions because histologically they are composed of variable quantities of fibrous and calcified tissues (Waldron, 1985). The radiology reflects the three histological stages of these lesions. The osteolytic stage represents the replacement of bone by fibrous tissue and is demonstrated by a well defined radiolucency. The cementoblastic stage, when cementum is generated within the fibrous tissue mass, features one or more radiopacities within the radiolucency. Finally, the mature stage, with the almost complete replacement by cementum, appears as large conglomerated opacity that may still be separated from adjacent normal bone by a radiolucent space (Shafer *et al.*, 1983). Once formed the lesions do not regress because cementum, unlike bone, appears to be resistant to osteoclasis (Waldron *et al.*, 1975). Dysplastic, haematogenous or neoplastic characteristics have been assigned to some of the cemental lesions (Punniamoorthy, 1980). Pindborg *et al.* (1971) separated the cemental lesions into four groups of which the benign cementoblastoma and cementifying fibroma are true neoplasms, whereas periapical cemental dysplasia (which affects the periapical areas of vital mandibular incisor and premolar areas) and gigantiform cementoma (which Waldron (1985) suggests is a more florid version of the former) are self-limiting. The term gigantiform cementoma has been occasionally replaced by terms that attempt to reflect its histopathology; florid osseous dysplasia (Melrose *et al.*, 1976) and florid cemento-osseous dysplasia (Waldron, 1985).

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Clinico-Radiological Material

Sixteen cases (mean age 52.1 years) are presented: six (Cases 1–6) of West Indian females (mean age of 54.2 years) and 10 (Cases 7–16) Chinese females (mean age of 50.9 years) who presented at King's College School of Medicine and Dentistry in London and Prince Philip Dental School in Hong Kong respectively. All cases were radiologically investigated either for pain from carious teeth or as part of a routine clinical assessment. Only two patients (Cases 6 and 7) exhibited a swelling that could be due to expansion by the cemental lesion of the buccal (external) and lingual cortices of the mandible.

All lesions were situated within the alveolar process; the lower border in the posterior areas was arbitrarily set as the inferior dental canal. Both the mandible and maxilla were divided into right and left posterior (molars and premolars) areas and an anterior (incisors and canines of both sides) area. The distribution of lesions within these areas is displayed in Table 1, which shows the bilateral nature of the lesions in the posterior areas of both jaws. The most common sites for the presence of these lesions were the posterior mandible followed by the posterior maxilla, anterior mandible and then the anterior maxilla.

On the radiograph more than one stage was frequently observed. One case exhibited the first stage (Fig. 1*b*, arrow), 13 the second (Fig. 2) and eight the third stage (Figs 3 and 4). The third stage was most frequently observed in the oldest women.

The lesions in two Chinese women were proven histologically.

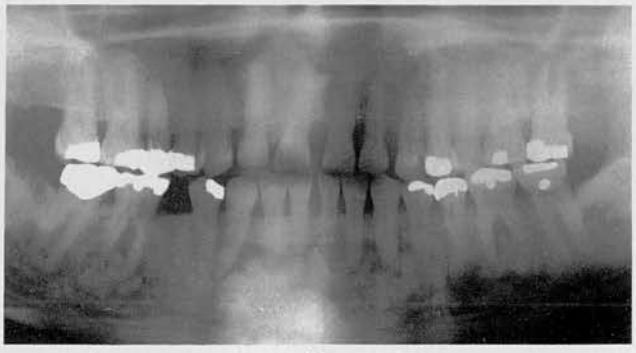
DISCUSSION

As the gigantiform cementoma has been predominantly reported in middle aged American Black women (Pindborg *et al.*, 1971; Waldron *et al.*, 1975; Melrose *et al.*, 1976), then this report of its occurrence in South London where a large Afrocaribbean population is resident may not be so remarkable, although only two cases have previously been reported in Britain (Millet, 1990; Lyons and Babajews, 1986). The surprising feature in this report is the large number of cases observed in the Hong Kong Chinese population. Until now the only oriental cases that appear to have been recorded are three Japanese women (Tanaka *et al.*, 1987) and nine Singaporean women (Loh and Yeo, 1989) with a mean age of 47 years.

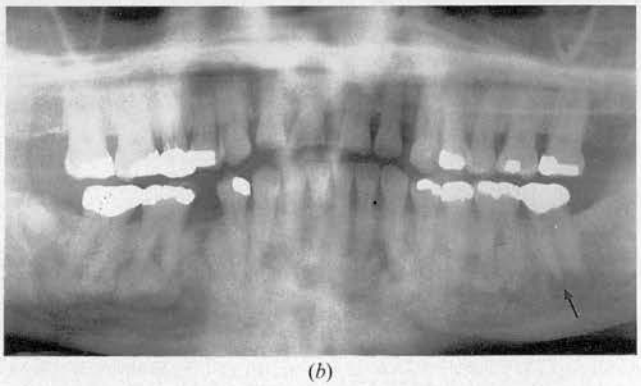
Table 1 – Distribution of lesions

Case no.	*Age* (years)*	*Mandible*			*Maxilla*		
		Posterior		*Anterior (–)*	*Posterior*		*Anterior (–)*
		R	*L*		*R*	*L*	
1	58	+	+	+	+	+	+
2	49	+	+	+	+	+	–
3	54	–	+	–	+	+	–
4	67	+	+	+	+	+	+
5	60	+	+	+	+	–	–
6	37	+	+	–	+	+	–
7	59	+	+	–	+	+	–
8	48	+	+	–	–	–	–
9	65	+	+	+	+	+	+
10	67	+	+	–	–	–	+
11	43	+	+	–	–	–	–
12	65	+	+	+	+	+	+
13	46	+	+	+	+	+	–
14	52	+	+	+	+	+	–
15	28	–	–	+	+	+	+
16	36	+	+	+	–	–	–
Total		14	15	10	12	11	6

* Age when the lesions were first observed radiographically.



(*a*)

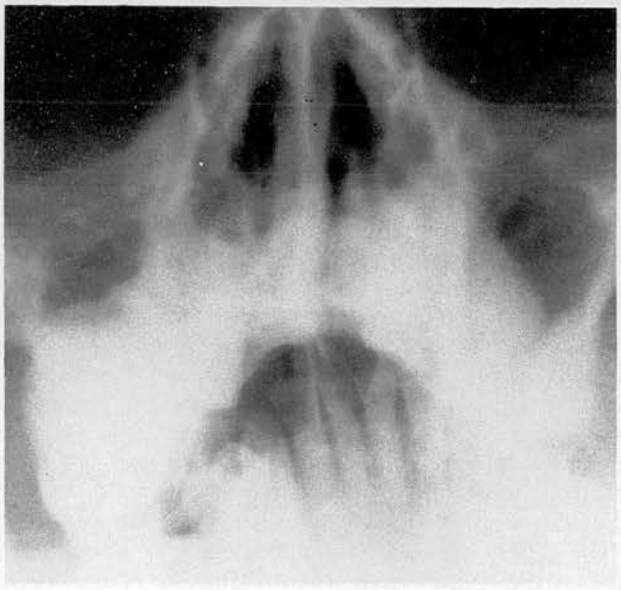


(*b*)

Fig. 1 – Case 1. (*a*) Opacities occurring within radiolucent areas associated with most mandibular and some maxillary teeth are demonstrated on a dental panoramic radiograph. (*b*) A radiograph taken 2 years later revealed increased opacification of these lesions, and a radiolucent area was also now apparent on the lower left third molar which may represent the earliest stage of a new lesion.

Fig. 2 – Case 6. Multiple opacities are seen on the panoramic radiography associated with almost all mandibular teeth. A radiopacity was observed within a radiolucent area in the left maxillary tuberosity. Additionally, a large spherical radiolucency 2 cm in diameter was associated with the lower left third molar tooth root, containing a central opacity. An occlusal film of this lesion demonstrated buccolingual expansion.

(*a*)



(*b*)

Fig. 3 – Case 4. (*a*) The dental panoramic radiograph demonstrates opacities associated with all mandibular and posterior maxillary teeth. (*b*) On the occipitomental projection the maxillary opacities are superimposed on the base of the antrum.

The cause of the gigantiform cementoma is still unknown, but a genetic cause is likely. The best evidence for familial transmission is derived from caucasian kindreds in which males (Sedano *et al.*, 1982) and younger individuals (Young *et al.*, 1989) are also frequently affected. The gigantiform cementomas in caucasians are more likely to exhibit an exuberant growth producing a marked deformity that frequently requires surgery (Cannon *et al.*, 1980; Lucas, 1984; Young *et al.*, 1989) and are therefore quite different to their presentation in individuals of negroid or of Chinese origin.

The clinical importance of this lesion to the dentist is that it complicates extraction of teeth and the provision of dentures, whereas to the general radiologist the main problem is likely to be diagnostic, as gigantiform cemen-

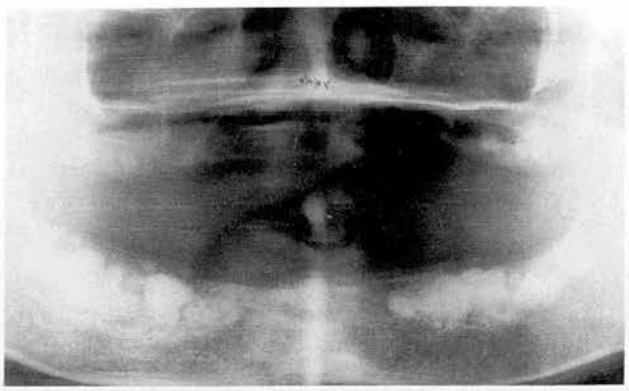


Fig. 4 – Case 7. Multiple dense radiopaque masses occupy the alveolar bone of the molar-premolar regions, bilaterally. In this edentulous patient a radiolucent zone separates these opacities from the adjacent bone. Small radiopaque masses are also visible in both posterior regions of the maxilla.

tomas occur predominantly in the older age group in which malignant neoplasms and Paget's disease are more common. Some metastatic deposits, especially from the breasts, can result in sclerotic lesions in the jaws, although metastasis to the jaws is not common. The symmetrical 'cotton wool' appearance of the gigantiform cementoma can mimic Paget's disease (Winer *et al.*, 1972), an osteodystrophy common in Britain especially in caucasians (Bennett, 1988) but rare in the Far East (Jacobs and Renton, 1987). Although 10–20% of all Paget's cases are monostotic (Jacobs and Renton, 1987) those affecting the mandible appear to be rare as only a few cases have been reported in the literature (Smith, 1978; Ellis and Connole, 1985; Camarda *et al.*, 1989). While it causes expansion of the alveolar bone and spacing and displacement of teeth (Otis *et al.*, 1986) the radiological presentation of Paget's disease affecting the jaws is similar to that seen elsewhere in the skeleton, with generalized change within the affected bone. This change would be visible in the basal portion of the mandible in addition to the alveolar portion, whereas the gigantiform cementoma is generally confined to the alveolar portion of one or both jaws. This is a valid diagnostic point as Waldron and Giansanti (1973) found that only three out of their review of 65 cases of fibro-osseous lesions extended beyond the alveolar bone. Surgical biopsy is not indicated for this lesion not only because of its classical appearance but also because the post-operative sequelae of infection and resultant deformity of the alveolar ridge may create problems with dentures.

The gigantiform cementoma has no other associations other than simple bone cysts (Melrose *et al.*, 1976; Waldron, 1985; Horner and Forman, 1988) and other cemental lesions (Young *et al.*, 1989) while osteomyelitis may be a frequent complication, especially of the avascular mature lesion (Waldron *et al.*, 1975). The increasingly widespread use of panoramic radiography not only in general dental practice but also in diagnostic radiology departments may explain why this lesion is becoming apparent in different populations. Therefore, it would be of great interest to assess the true prevalence of this lesion in various world populations as a prelude to identifying its cause, sequelae and associations.

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Florid osseous dysplasia in Hong Kong Chinese

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Objectives. To report the radiological features of florid osseous dysplasia (FOD) in a Chinese population.
Methods. Twenty-three cases of histologically confirmed FOD affecting middle-aged Hong Kong Chinese women were reviewed.
Results. Sixteen patients presented with symptoms arising from the lesions. Twelve cases exhibited bilateral lesions, five were in both the upper and lower right quadrants, and there were six cases of a solitary lesion; the mandible was affected twice as frequently as the maxilla. Whereas all bilateral and unilateral lesions were provisionally diagnosed as FOD, all six solitary (localized) cases were thought to be other entities. There was a significant association between edentuous areas and FOD lesions.
Conclusions. While the radiological presentation of FOD in this series of Chinese women appeared similar to that reported in Western populations of Negroid origin, the greater prevalence of symptoms in the former may arise from secondary infection of the FOD lesions due, until recently, to the lack of availability of formal dental care.

Keywords: panoramic radiography; jaw abnormalities; fibrous dysplasia of bone; jaw diseases

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Florid osseous dysplasia (FOD) is a well-recognized condition affecting middle-aged women of Negroid origin[1] with a prevalence as high as 5%[2]. The term was first applied by Melrose *et al.*[1] to a condition in which there were exuberant multiquadrant masses of cementum and/or bone, and this term is now preferred to the original name of gigantiform cementoma[3].

FOD belongs to the group of diseases called fibro-osseous lesions because histologically they are composed of variable quantities of fibrous and calcified tissues[4]. The radiological appearances reflect the sequence of the pathological process from the initial osteolytic stage, represented by a well-defined radiolucency, through to the mature stage, where, due to the almost complete replacement of fibrous tissue by cementum, the FOD appears as one or more large conglomerated opacities that may be separated from adjacent normal bone by a radiolucent space[5].

This paper presents the radiological features of 23 histologically confirmed cases of FOD in Hong Kong Chinese women.

Materials and methods

The clinical notes, radiographs and histopathological reports of 23 histologically confirmed cases of FOD in Hong Kong Chinese women treated at the Dental School of the University of Hong Kong over the last ten years were retrospectively reviewed. The patient's sex, age, clinical history and findings on examination, and the differential or provisional diagnosis were obtained from the clinical notes. The radiographs were viewed by the author on a standard viewing box. Dental panoramic radiographs (Panelipse, GE, Milwaukee, USA) were available for all cases, and, in some cases, periapical and occlusal views were available. FOD classified as bilateral, unilateral or solitary. The histological diagnosis was based on the presence of mineralization that exhibited features of cementum within the fibrous tissue mass of the FOD.

Results

The results are summarized in Table I. The women had a mean age of 59.4 years (sd 11.2; range 37 to 83). Sixteen patients presented with symptoms arising from the lesions; the rest were incidentally observed on radiological investigation prior to the provision of fixed or removable protheses.

Whereas bilateral radiopacities, some exhibiting a translucent zone (Figures 1a and 1b) were observed in 12 patients (age 62.7 years; sd 11.2), five patients had

Table I Distribution of 23 cases of florid osseous dysplasia

Case no.	Age (years)	Symptom	Mandible			Maxilla		
			Posterior		Anterior	Posterior		Anterior
			R	L		R	L	
Bilateral								
1	73	P	+E	+	+	+	−	+
2	59	PS	+E	+E	+E	+E	+E	−E
3	67	PS	+E	−E	−E	+E	+E	−E
4	43	P	+	+	+	−	−	−
5	60	P	+	+	−	−	−	−
6	65	Nil	+	+	+	+E	+E	+
7	55	P	+E	+	+	+	+	+
8	68	PD	+	+	+	+E	+E	+
9	65	Nil	+	+	−	−	−	−
10	83	PS	+E	+	−	+	+	−
11	43	Nil	+	+	−	−	−	−
12	71	PS	+	+	−	−	−	−
Unilateral								
13	68	Nil	+	−	+	+E	−	−
14	54	P	+	−	−	+	−	−
15	54	P	+	−	−	+	−	−
16	59	D	+E	−E	−	+E	−E	−
17	69	Nil	+E	−E	−	+E	−E	−
Solitary								
18	65	P	−	+E	−	−	−	−
19	45	Nil	+E	−	−	−	−	−
20	60	P	+E	−	−	−	−	−
21	42	P	+E	−	−	−	−	−
22	60	Nil	−	+E	−	−E	−	−
23	37	N	+E	−	−	−	−	−

P, pain; S, swelling; D, discharging sinus; N, numb lip.
E, edentuous areas.
+: present, −: absent

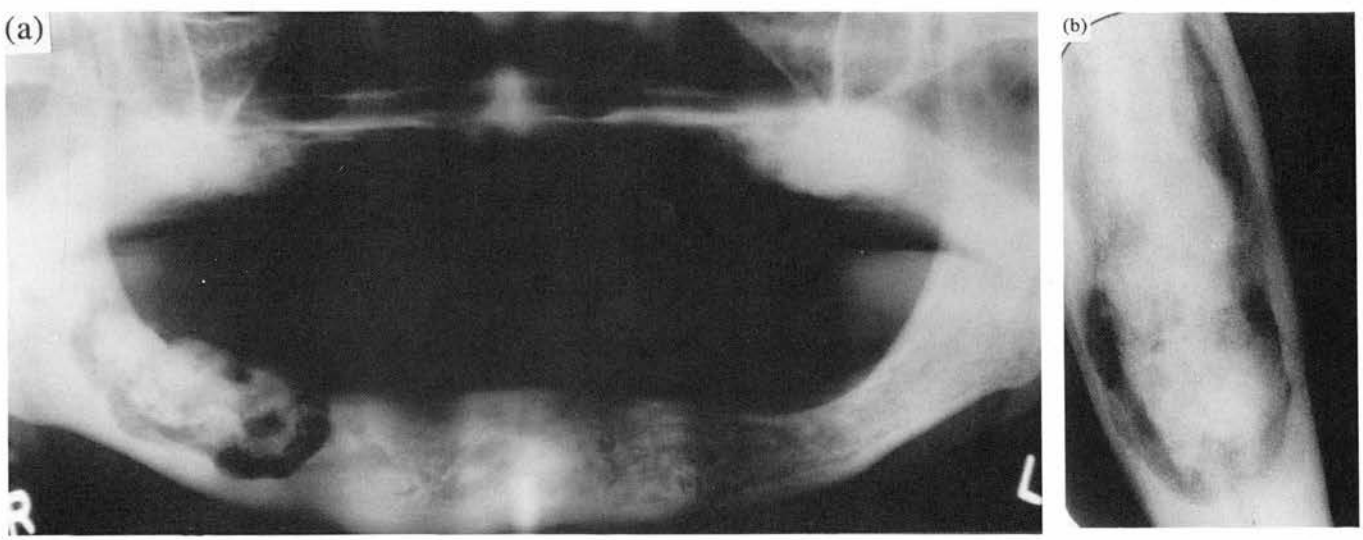

Figure 1 (a) A panoramic radiograph (case 3) showing FOD involving both upper molar areas and the lower right molar–premolar area. The latter area exhibits a wide translucent zone between the opacity and the adjacent bone. (b) No significant expansion is evident on the true occlusal view of the lesion in the lower right quadrant: the wide translucent zone is again clearly demonstrated.

unilateral lesions in both jaws on the right side only (age 60.8 years; sd 6.6); a solitary lesion was found in a further six patients (age 51.5 years; sd 10.6). The patients with a solitary FOD tended to be significantly younger than those with bilateral lesions ($t = 2.67$; 17 d.f.; $p < 0.05$). The mandible was affected twice as frequently as the maxilla.

All patients with bilateral or unilateral lesions were provisionally diagnosed by the receiving clinician or the oral surgeon as FOD, whereas the provisional diagnoses in the six patients with solitary FOD were four as cementoblastomas, one as an odontoma and the other as osteomyelitis. Osteoma and calcifying cyst were also occasionally included in the differential diagnosis.

A significant association was observed between

edentuous areas and FOD ($\chi^2 = 15.2$; 1 d.f.; $p < 0.001$). This association was greatest for the solitary lesions.

Discussion

Waldron established that there were two manifestations of FOD: the generalized form giving rise to the classical multiquadrant presentation and the localized (or solitary) form confined to one site[4]. FOD has been predominantly reported in middle-aged women of Negroid origin in America[1,2,6] and the UK (eight patients reported in total; six by MacDonald-Jankowski[7] and one each by Lyon and Babajews[8] and by Mille[9]). The large number of classical cases reported here supplements other reported cases of generalized FOD affecting over 20 oriental middle-to-older-aged women of Japanese[10], Singaporean[1] and Chinese origin[7]. The mean age of the bilateral cases in this paper is older than that in the last of these reports[7] which was based on radiological identification alone. In contrast, the solitary form tends to affect younger individuals, in agreement with Neville and Albenesius[2]. Additionally, since the patients with the unilateral lesions are relatively younger, it may well be that the solitary lesions progress to unilateral and in turn to bilateral forms with increasing age. The predilection of the solitary and unilateral cases of FOD for the right side in this report is in contrast to the four cases in the left side of the mandible described by Higuchi *et al.* for women with a mean age of 40 years[12]. More reports may help to substantiate both this apparent predilection for the right side and also the trend to multiple-quadrant involvement with advancing age.

The solitary form of the lesion was included in this study, as it appeared to have been included in the spectrum of fibro-osseous lesions reported in a relatively non-specific fashion by Neville and Albenesius in their radiographic survey of 1138 black women[2]. Although as many as 41 out of their 63 fibro-osseous lesions were confined to a single quadrant, only eight were biopsied. As a general rule, a definitive diagnosis should not be made on radiological criteria alone, in particular for the solitary form of FOD, as shown by the range of differential diagnoses found in this study.

Whereas all of Loh and Yeo's[11] nine cases presented with symptoms, this was the case in only 16 out of the 23 cases in the present study. On the other hand, these results are at variance with those of Melrose *et al.*[1] who reported that only ten out of their 34 cases had any symptoms. An explanation for this difference could be that a larger proportion of cases in the present study had become secondarily infected, thus producing pain, swelling and numbness.

This report confirms Waldron's[4] observation that solitary FOD is localized in particular to edentuous areas of the posterior mandible, and this may also be seen to a lesser degree for the generalized lesions. Therefore, since many occur at sites of previous extraction, they may partly represent, as suggested by Waldron[4], the end-stage of an abnormal reaction of bone to injury.

This working-class Chinese population differs from the other large reported series, particularly that described by Melrose *et al.*[1], in that it may approximate to that of a developing world population, so far not reported. A formal dental profession was only established in Hong Kong after the Second World War, and the current population, which is essentially composed of post-war, mainland Chinese immigrants, predominantly of peasant or fishing origin, has, largely, not experienced regular dental care[13,14].

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Histogram-matching and histogram-flattening contrast correction methods: a comparison

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Objectives. To compare the results of two methods of histogram matching and two methods of histogram flattening for their ability to correct for contrast variations in digital dental images.
Methods. A custom-built, aluminium stepwedge with 0.1, 0.5 and 1.0 mm steps was placed over Ektaspeed films and exposed for 0.06, 0.12 and 0.25 s, respectively. Radiographs were digitized at 50 μm spatial resolution and 12-bit contrast resolution. Contrast corrections were performed using Rüttimann *et al.*'s algorithm (1986) for one method of matching (RM) and flattening (RF) and Castleman's algorithm (1979) for the other method of matching (CM) and flattening (CF). Mean pixel grey-scale values were determined for each step. The 0.12 s exposure was considered to be the target image exposure. Absolute differences in pixel grey-scale values between the target images and the modified images were determined.
Results. The median values of the absolute differences in pixel grey-scale values between the target images and the contrast corrected images were: CM = 4.3; RM = 4.1; CF = 70.2 and RF = 70.2.
Conclusion. Castleman's and Rüttimann's matching algorithms perform equally well in correcting digital image contrast. Histogram flattening was less effective.

Keywords: radiographic image enhancement; subtraction radiography; signal processing, computer-assisted

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Retrospective correction for variations in dental film exposure, film processing and radiograph digitization is an essential step in measurement of small changes in hard tissue[1–4]. In 1986, a non-parametric histogram-matching algorithm for making such corrections was introduced by Rüttimann *et al.*[5]. This method, which we refer to as Rüttimann's algorithm, has found wide acceptance in quantitative digital-imaging studies[6–9]. Additional algorithms have been reviewed, and those incorporating non-parametric contrast correction, similar to that described by Rüttimann, have performed best[10,11].

The first step in using the Rüttimann matching (RM) algorithm is to create a histogram for each of the digital images that are to undergo contrast correction. For each histogram, a running sum of the frequencies of pixels at each grey-scale value is calculated to yield a cumulative grey-scale distribution (cumulative density function; CDF). The cumulative sums of pixels at each grey-scale value in the input (original) image are matched to the corresponding cumulative sums of the target (desired) image. The result is that the cumulative sum of the desired image is less than or equal to the cumulative sum of the original image while also being greater than the next lower bin of the cumulative sum of the original image[5].

A similar approach to histogram matching contrast correction is integrated into the Mayo Clinic's ANALYZE™ program – a comprehensive software system of biomedical and scientific visualization applications[12,13]. The matching routine in this program is based on an algorithm described by Castleman in 1979[14]. With this algorithm, the CDF of the input image is forced to match as closely as possible that of the target image, and, as such, the algorithm is somewhat similar to that of Rüttimann's. Over the last two

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Cemento-ossifying fibromas in the jaws of Hong Kong Chinese

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Objective: To determine the clinical and radiological features of cemento-ossifying fibroma (COF) in a Chinese population.
Methods: Twenty cases of COF found in Chinese patients for whom the clinical notes, radiographs and histopathology reports were available, were reviewed to determine their clinical and radiological features. Overall size was measured digitally from the radiographs.
Results: All COFs occurred in females and most frequently in the third and fourth decades. Seventeen COFs were in the mandible and three in the maxilla. Eighteen COFs had well-defined margins and were round or ovoid in shape. Four were radiolucent and 15 mixed density. COFs tended to be smaller in women in their early to middle-40s and larger in older women.
Conclusions: The clinical and radiological features of this Chinese series were broadly consistent with those of non-Chinese populations reported previously. The principal difference was that all 20 patients were female.

Keywords: radiography, dental; neoplasms, connective tissue; bone neoplasms; odontogenic tumours

Introduction

The cemento-ossifying fibroma (COF) is a benign neoplasm which is generally slow-growing. Although it has principally been found in the jaws, it has also been reported in the frontal, ethmoid, sphenoid,[1] temporal[2] bones and in the orbit, in the anterior cranial fossa.[3] The COF exhibits a variable behaviour ranging from slow growth to aggressive local destruction; some cases recur after surgery.[4] This variable behaviour cannot be predicted on the basis of the histopathology which is itself variable.[5]

The histopathology revealed a characteristically encapsulated lesion with a highly-cellular, predominantly fibroblastic, stroma in which woven bone formation occurs.[6] The previous nomenclature of ossifying fibroma or cementifying fibroma was based upon the histopathology which displayed predominately bone-like or cementum-like tissue, characterised by osteoblasts and cementoblasts respectively. This terminology was first used by Hamner *et al*[7] but is of little practical value because of the range of the behaviour of these lesions with identical histopathological appearance. Furthermore, many of them contained both bone- and cementum-like elements. Therefore these lesions appear to represent points on a spectrum of histological appearances extending from bone to cementum. This indicates that they probably arose from the same progenitor cell, which Waldron[8] suggested is to be found within the periodontium. Taking account of the wide range of histological manifestations, the WHO in 1992 revised its nomenclature to refer to the hitherto separate lesions of the cementifying fibroma and the ossifying fibroma as a single entity termed the cemento-ossifying fibroma.[8]

The classical three stages in the radiographic appearance of the COF, like other fibro-osseous lesions, generally reflects the underlying histopathology, which in turn depends on the maturity. The initial appearance is radiolucent, which then becomes progressively more radiopaque as the stroma mineralises. Eventually, the individual radiopacities coalesce to the extent that the very mature lesion may appear sclerotic. COF unlike florid osseous dysplasia (FOD) is solitary and unlike the cementoblastoma is infrequently associated with root resorption.

Although a series of COFs in 11 Hong Kong patients has already been reported by Wu *et al*,[9] this was essentially part of a histopathological analysis of jaw tumours with no reference to their radiological or clinical features. The aim of this report is to review the radiological and the principal clinical features of a

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further group of 20 cases occuring in Hong Kong Chinese and to compare these findings with those of other populations.

Materials and methods

The pathological files of the Dental School of the University of Hong Kong between 1982 and 1992 revealed 20 cases of COF affecting the jaws for which the clinical notes and radiographs were available. The definitive diagnosis of a COF was made on the basis of both the histopathology and the radiology. Each COF was radiographed in two planes. A panoramic and periapical radiograph were available for all cases. Every mandibular case was accompanied by a true occlusal and oblique anterior radiographs were available for all lesions in the anterior region in both jaws. Occipitomental and lateral sinus views had been obtained for the two cases involving the maxillary antrum. The radiographs were viewed on a standard illuminated screen and assessed by a single investigator (DM-J). The influence of the COF on adjacent structures, such as the teeth, the buccal and lingual cortices, lower border of the mandible and the maxillary antrum, was noted. The outline of the COF was defined as the well-defined boundary between the normal adjacent bone and the lesion. The margin of any poorly-defined lesions was subjectively taken to be the point at which the bone at this margin appeared indistinguishable from the adjacent normal bone. The outline of the COFs was then traced by the cursor of an image analyser (Kontron Bildanalyzer, Carl Zeiss Far East Co. Ltd., Hong Kong) and the area expressed in cm^2.

The measurements were made directly from either the intra-oral or panoramic radiographs. Although periapical radiographs were available in every case, they were not generally used for measurement because of their frequent inability to encompass fully the whole lesion. Therefore most of the measurements were made from the panoramic and standard anterior occlusal radiographs; the latter were exclusively used for lesions anterior to the canines. The values obtained from the panoramic radiographs were corrected for the measured values derived from it had to be adjusted a magnification factor of 1:1.2 (Panelipse, GE, Milwaukee, USA). Observer self-calibration was achieved by comparing values derived for measurements produced on two separate occasions; the reproducibility was in excess of 95%. Student's *t*-test and X^2 test were used for the statistical analysis.

Results

The details of the size and distribution of the twenty COFs (17 in the mandible and three in the maxilla) are shown in Table 1 and their clinical and radiological features in ascending order of age in Table 2. All 20 patients were female with a mean age of 39.3 (s.d. 13.9) years. The distribution of the 20 cases according to age is set out in Table 1; most cases were found in the third and fourth decades.

Ten lesions (50%) occurred in the posterior mandible, seven (35%) in the anterior mandible, two (10%) in the posterior maxilla and one (5%) in the anterior maxilla (Table 1). Eleven lesions were observed as incidental findings on panoramic radio-

Table 1 The gender and age of 20 patients with cemento-ossifying fibromas together with the size and site of the lesions. Teeth are numbered 8 (third molar) to 1 (central incisor). The dotted line between the bars indicates the extent

Case				*Right*								*Left*							
No.	*Gender*	*Age (yrs)*	*Size (cm^2)*	*8*	*7*	*6*	*5*	*4*	*3*	*2*	*1*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
Mandible																			
1	F	21	4.15											I	I				
2	F	26	10.15					I							I				
3	F	28	1.44						I	I									
4	F	29	11.12												I				I
5	F	33	1.39		I	I													
6	F	35	3.01			I	I												
7	F	37	2.48					I	I										
8	F	38	1.77			I	I												
9	F	39	1.42		I	I													
10	F	39	1.54													I	I		
11	F	48	1.77							I			I						
12	F	48	1.77										I	I					
13	F	50	7.70													I			I
14	F	52	8.24						I					I					
15	F	52	4.90			I													
16	F	55	1.59								I	I							
17	F	80	3.80							I			I						
Maxilla															Left				
18	F	26	N/A												I				I
19	F	33	1.18								I	I							
20	F	44	4.09												I		I		

Table 2 The clinical and radiological features of 20 cases of cemento-ossifying fibroma

Case no.	*Signs and symptoms*	*Provisional diagnosis*	*Radiological features*					
					Periphery definition		*Inf. border mand.*	
Mandible			*Shape*	*Opacification*	±cortex	*Expansion*	*Displaced*	*Thinned*
1	Incidental finding	Nil	round	light opaque centre	well-defined + cortex	Yes	Yes	No
2	Loose lower teeth	ameloblastoma	multiloc.	radiolucent	well-defined + cortex	Yes	No	No
3	Incidental finding	Nil	round	opaque centre	well-defined + cortex	No	No	No
4	Gradual swelling of lower left jaw	Nil	ovoid	radiolucent	well-defined	Yes	Yes	No
5	Incidental	OF cem.bl.oma	round	opaque centre	ill-defined	No	No	No
6	Swelling	Nil	round	radiolucent	well-defined + cortex	Yes	No	No
7	Incidental	cementoblastoma	round	opaque centre	well-defined + cortex	No	Yes	Yes
8	Incidental	Nil	lobular	opaque centre	well-defined + sclerotic margin	No	Yes	Yes
9	2-year swelling	Nil	round	radiolucent	well-defined	Yes	No	No
10	Incidental	chronic sclerosis osteomyelitis	round	3 round opacities	well-defined + sclerosis + cortex	No	No	No
11	Incidental	Nil	ovoid	opaque centre	well-defined	No	No	No
12	Referred with 10 year swelling + pain on chewing	Nil	round	opaque centre	well-defined	Yes	No	No
13	Incidental Hard swelling	osteoma or FOL	ovoid	many opacities	well-defined	Yes	No	No
14	Incidental	OF	ovoid	opaque centre	well-defined	Yes	No	No
15	Pain	FOL	round	opaque centre	well-defined	Yes	Yes	Yes
16	Pain, swelling and ulcer	cementoblastoma	ovoid	2 round opacities	well-defined	Yes	No	No
17	Nil	OF odontoma	ovoid	opaque centre	well-defined	Yes	No	No
Maxilla							*Affects antrum*	
18	Nil	FOL odontoma	N/A	dense Lt Antrum	well-defined	Yes	Yes	
19	Sensitivity to cold. Incidental	Nil	Ovoid	ovoid + cortex	well-defined	Yes	No	
20	Incidental	FOL	ovoid	opaque	well-defined + cortex	Yes	No	

Nil = no provisional diagnosis provided. FOL = Fibro-osseous lesion. OF = ossifying fibroma

graphs prescribed for the assessment of common dental problems such as third molars, toothache and periodontal disease (Table 2). Only one of the four referred patients had been specifically referred by her general dental practitioner for investigation of the symptoms and signs associated with the COF (Table 2; Case No. 12). Five mandibular lesions were associated with swelling alone and two with pain alone; a further case was accompanied by both swelling and pain. The three cases associated with pain occurred in the oldest patients (Table 2).

A provisional diagnosis was available in 11 cases. Four lesions were provisionally identified as an 'fibro-osseous lesion' and three as cementoblastomas, two as odontomas and one each as osteoma, chronic sclerosis osteomyelitis and ameloblastoma. Of the three cases where 'ossifying fibroma' was considered in the provisional diagnosis, only in one case was it offered as the sole possibility (Case No. 14).

Generally, the COFs appeared radiographically as well-defined unilocular round or oval structures (Figure 1). Thirteen mandibular and two maxillary COFs presented with central radiopacities (Figure 2). The remaining maxillary case presented as a dense opacification. The four radiolucent lesions occurred in the younger patients. Eighteen of the COFs possessed well-defined peripheries additionally eight had a sclerotic 'cortex', further delineating the COF from the adjacent normal bone. These eight cases were confined to the third and fourth decades. Fourteen lesions exhibited buccolingual expansion (Figure 3); in the mandible, it was present in all of the five oldest cases (Cases No. 13 to 17) and three of the youngest five cases (Cases No. 1 to 5) whereas only one such

case was observed in the middle five (Cases No. 7 to 11). Five mandibular lesions, (all in the posterior quadrant), presented with downward displacement of the inferior border of the mandible; three were also associated with its thinning (Figure 1). Displacement of adjacent roots occurred in three cases. Both COFs sited in the posterior quadrant of the maxilla had expanded upwards into the maxillary antrum.

The overall mean size of the 19 lesions which could be measured from the radiographs was 3.91 (s.d. 3.04) cm^2. Case 18 was excluded because the radiograph was not available for the second calibration measurement. The five youngest and five oldest mandibular cases (Cases No. 1 to 5 and Cases No. 13 to 17 respectively) were larger (means 5.65 (s.d. 4.2) and 5.25 (s.d. 2.47) respectively) than the middle five cases (Cases No. 7 to 11; mean 1.89 (s.d. 0.53)). The difference between the oldest five and the middle five tended to significance ($t=3$; $0.025>P>0.01$), whereas the difference between the youngest five and middle five was not significant ($t=1.99$; $0.1>P>0.05$).

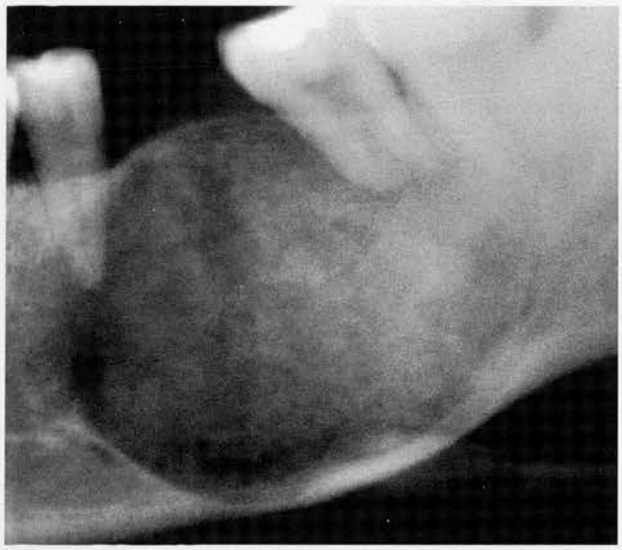

Figure 1 (Case 4). Part of a panoramic radiograph, showing a large oval, mixed-density lesion extending throughout the length of the posterior part of the body of the left mandible. At the periphery there is a clearly defined transitional zone which is enhanced in places by a sclerotic margin. The lower border of the mandible been substantially displaced and thinned

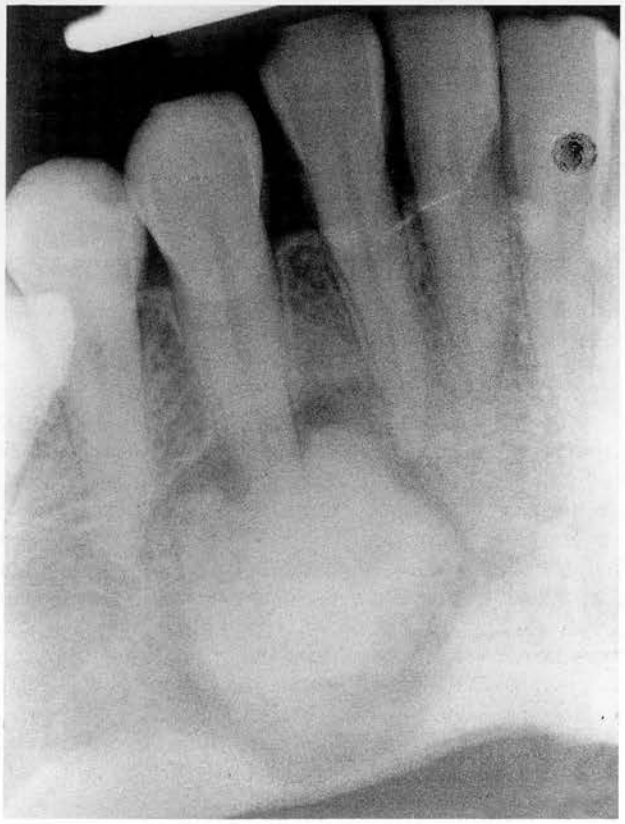

Figure 2 (Case 7). A periapical radiograph of a lower right first premolar. The apex is associated with an irregular, radiopaque mass, which is separated from the adjacent normal bone by a well-defined radiolucent margin. There is no evidence of root resorption

Discussion

The findings in the present study that COF is more prevalent in females (70%) and in the mandible (75%) are consistent with previous reports (Table 3)[5,7,9–16]. The exclusive preponderance of females in this series is not only an extreme case of this trend, but more specifically confirms the high female predilection in the only other report on this population by Wu *et al.*[9] This predilection for females is statistically significant when compared with the 31% : 69% male:female ratio seen in the other 377 non-Hong Kong cases ($X^2=9.2$; $P<0.005$). The complete absence of males in this series may be explained by reference to Table 4.[5,13,15,16] The percentage of males falls from 71% and 41% for the first and second decades respectively to 14% and 15% for the third to fourth decades. In contrast 20

Figure 3 (Case 7). A true occlusal radiograph showing that the irregular central opacity seen in Figure 2 is associated with substantial expansion of the lingual plate which has been significantly thinned. Similar changes can be seen in the buccal plate. The apex of the first premolar has been displaced buccally

Table 3 A summary of series of cases of cemento-ossifying fibroma reported in various ethnic groups*

Author(s)	*Ethnic group*	*Number of cases*	*Male: Female*	*Age mean (range) (years)*	*% Swell.*	*Signs and symptoms % Pain*	*Other*	*Maxilla: mandible*
Anand *et al*[10]	Nigerian	19	6:12 (1 unknown)	26(12–44)	100%	30%	16 teeth displaced & 2 proptosis	10:9
Hamner *et al*†	US (75%W; 20%B; 4%O)	67(CF)	IIG	IIG	ING			16:51
	US (70%W; 28%B; 2%O)	57(OF)	31:26	26(7–58)	IIG			17:39
	US (69%W; 31%B)	42(COF)	13:29	32(5–71)	IIG			10:32
Regezi *et al*[11]	US(ING)	11	2:9	40(18–75)	ING			1:9
Sweet *et al*[12]	US(ING)	94	ING	ING	ING	97%		21:73
Eversole *et al*[5]	US (50%W; 16%B; 21%H; 10%O; 3%A)	64	12:52	36	*few swelling, majority incidental*			7:57
Wu and Chen[9]	Hong Kong (100%O)	11	1:10	40	ING			4:7
Sciubba and Younni[13]	US (14W:; 2B; 2H)	18	7:11	30	ING			4:14
Slootweg and Muller[14]	Holland (ING)	12	8:4	25	ING			5:7
Summerlin and Tomich[15]	US (60%W; 22%B; 11%H)	45	15:30	30	*frequently painless swelling*			13:32
Su *et al*[16]	US (53%W;; 38%B; 3%H; 3%O; 3%A)	75	18:57	32(10–59)	51%			22:53
Present	Hong Kong (100%O)	20	0:20	39(21–80)	30%	15%	11 incidental	3:17
Summary	(56%W; 26%B; 5%H; 10%O; 1%A)	535	111(30%):260(70%)	31yrs (mean age of 376 cases)	57%	75%		133:400 (25%):(75%)

W = white; B = black; H = hispanic; O = oriental; A = amerindian. ING = information not given. IIG = imprecise information given. *only those reports which clearly differentiate between fibrous dysplasia and COF have been included. †reported the three common manifestations of COF, (CF cementifying fibroma, OF ossifying fibroma and COF as separate lesions)

cases in this report occurred in the third decade and above. Furthermore, the absence of COF in younger patients of either sex may be due to the early lesion having been misdiagnosed as periapical lesions or odontomas.

It can be seen from Table 3 that the clinical presentation is variable; all individuals in the Nigerian series[10] presented with swelling, almost all with tooth displacement and a third with pain, whereas the majority of individuals in an American (inner-city/urban) population[5] were symptom-free and therefore the lesion was discovered incidentally. The fact that eleven cases in the present study were discovered incidentally and only eight cases were associated with swelling and/or pain, places it between the extremes in clinical presentation of these two populations. This would be consistent with the intermediate socio-economic status of Hong Kong and the related degree of availability of dental care in the 1980s.

The order of site prevalence in the present study is similar to that observed in other reports (Table 5)[5,7,11,13,16] the posterior mandible (61%), the anterior mandible (17%), the posterior maxilla (15%) and the anterior maxilla (7%).

The radiographic features of COF reported in the literature vary markedly (Table 6).[13,16,17] The majority of those in the present report were well-defined mixed density lesions, whereas most of those described by Sciubba and Younai[13] were radiolucent. A reason for this difference may be that the mean age of the latter cases[13] was younger than in the present study. The radiological appearance of the COF depends upon its maturity. Table 7 would appear to confirm this; the study with the youngest mean age reports a higher proportion of radiolucent lesions,[13] whereas the present report with the oldest mean age recorded the lowest. Furthermore, the appearance of complete radiolucencies only in the younger cases suggests that calcification will occur increasingly with age.

Table 6 also shows that while 93% of COFs have radiographically well-defined borders, this feature was accompanied by marginal sclerosis and a thin cortex[18] in only half of these cases. Table 2 shows that cortication is found in the third and fourth decades. Its presence is usually taken as indicative of a slow growing or relatively static lesion. Therefore, the absence of such a feature in the older patients suggests that these may be growing more rapidly.

Seventy percent of the cases in this study had buccolingual expansion, consistent with the 72% reported by Sciubba and Younai.[13] Vertical expansion was also seen in the present report. Downward displacement of the lower border of the mandible, seen in 29% of cases, has not previously been reported. Eighty-six percent of COFs show expansion into the maxillary antrum (Table 6). This overall value was derived from the present study and from Sciubba and Younai,[13] the only other authors to specify this feature. Antral involvement can on occasion be very substantial; Sciubba and Younai[13] reported two cases which reached the floor of the orbit.

Although the smaller size of the lesions in women in their mid-40s was unexpected, this difference may

Table 4 The distribution of cases of cemento-ossifying fibroma according to age (in decades) in the present report and in the literature. The number of male and female cases are in parentheses

Decade	*Eversole et al*[5]	*Sciubba and Younai*[13]	*Summerlin and Tomich*[15]	*Su et al*[16]	*Present study*	*Total*	*Percentage*	*Males %*
1st	1 (1:0)	1 (1:0)	1	12 (8:4)	0	15 (10:4)	7	71
2nd	8 (2:6)	5 (2:3)	9	19 (9:10)	0	41 (13:19)	18.5	41
3rd	18 (4:14)	3 (1:2)	15	25 (2:23)	5 (0:5)	66 (7:44)	30	14
4th	18 (2:16)	3 (1:2)	8	12 (3:9)	7 (0:7)	48 (6:34)	22	15
5th	8 (1:7)	4 (1:3)	6	7 (1:6)	3 (0:3)	28 (3:19)	13	14
6th	8 (0:8)	1 (0:1)	3	0	4 (0:4)	16 (0:13)	7	0
7th	3 (2:1)	1 (1:0)	0	0	0	4 (3:1)	2	75
8th	0 (0:0)	0 (0:0)	0	0	0	0		
9th	0 (0:0)	0 (0:0)	0	0	1 (0:1)	1 (0:1)	0.5	0
Total	64 (12:52)	18 (7:11)	42	75 (23:52)*	20 (0:20)	219 (42:135)	100	

*These male:female proportions differ markedly from those given by Su *et al*[16]

Table 5 Distribution of the cases of cemento-ossifying fibroma reported in the present study and the literature, according to the site

	Maxilla: Mandible	*Maxilla*		*Mandible*	
		Anterior	*Posterior*	*Anterior*	*Posterior*
Hamner *et al*[7]	(COF) 10:29	3	7	8	21
	(OF) 10:26	6	4	4	22
Regezi *et al*[11]	1:9	1	0	0	9
Eversole *et al*[5]	7:57	4	3	11	46
Sciubba and Younni[13]	4:14	1	3	3	11
Su *et al*[16]	22:53	3	19	12	41
Present study	3:17	1	2	7	10
Summary	57:205	19 (7%)	38 (15%)	45 (17%)	160 (61%)

COF = cemento-ossifying fibroma; OF = ossifying fibroma

Table 6 Summary of the radiological features in 177 reported cases of cemento-ossifying fibroma

	Number of Cases	*Radiodensity*			*Well-defined*	*Margins or corticated*	*Bucco-linqual*	*Expansion*	*Antral involvement*	*Root*	
		Lucent	*Opaque*	*Mixed*				*Lower border of mandibular*		*Resorption*	*Displace-ment*
Eversole *et al*[17]	64	20	11	33	64 (100)	ING	10+	ING	ING	7	11
Scuibba and Younai[13]	18	10	1	7	18 (100)	ING	13	ING	4*	8	6
Su *et al*[16]	75	40	30	5	64 (85)	34	ING	ING	ING	ING	ING
Present study	20	4	1	15	18 (90)	8	14	5	2	0	3
Total	177	74 (42)	43 (24)	60 (34)	164 (93)	42 (44)†	>37 (>37)	5 (39)	6 (86)	15 (15)	20 (20)
		177									

ING = information not given. IIG = inprecise information given. *includes two COFs which were so large that they reached the floor of the orbit. + it is likely that more cases in this report may have exhibited buccolingual expansion. † = 51% of 82 well-defined cases. The numbers in parentheses are the percentage of the total number of cases

disappear with the reporting of more cases, otherwise the difference between the middle- and older-aged groups approached significance. This would suggest that COFs may arise, or their growth may be reactivated, in middle-to-old age. Further support for this notion is derived not only from the absence of cortification in the middle-to-old aged patients, but also from the distribution of buccolingual expansion with age. Buccolingual expansion was most prevalent in the five oldest cases (five cases) but least in the middle five (one case), whereas it was intermediate in prevalence in the five youngest (three cases). These features suggest that a hormonal change could be responsible for triggering the growth of COFs in later life. This effect has been considered for the growth of fibrous dysplasia in pregnancy.[19] Details of the patients' gynaecological and obstetric history were however not recorded in the clinical dental notes.

The differentiation between the COF and fibrous dysplasia is very difficult on the basis of both the clinical and histopathological features. The erroneous view that both lesions are part of the same spectrum still appears to persist in some quarters.[20] Differentiation is, in most cases, dependent on the radiographic

Table 7 Summary of the relationship between the number of cases in the literature and the present study with a radiolucent cemento-ossifying fibroma and the mean age

	Number	*Mean Age (years)*	*Radiolucencies number (per cent)*
Sciubba and Younai[13]	18	30	10 (56)
Su *et al*[16]	75	32	40 (53)
Eversole *et al*[17]	64	36	20 (31)
Present study	20	39	4 (20)

appearances. The presence of a well-defined margin was held by Sciubba and Younai[13] to be a consistent and reliable radiological marker for COF. A COF was only considered in three of the 11 cases where a differential diagnosis was offered by the receiving surgeon or referring general dental practitioner. This is particularly surprising when the cementoblastoma which is a much rarer lesion, with only 70 reported cases,[21] was also considered in three cases. In addition to its rarity, root resorption, an important diagnostic feature of cementoblastoma, was completely absent in the present study.

The COF is treated by surgical enucleation, but continued growth does not necessarily follow if the tumour is only partly removed.[22] Nevertheless, Eversole *et al*[5] reported a 28% recurrence rate following curettage in 22 patients followed up over 38 months. They could not detect any radiological features which could predict a recurrence. In the absence of a reliable diagnostic or prognostic predictor to indicate the potential of COF for aggressive behaviour or likelihood of recurrence, then long term follow-up should include radiology.

Other lesions with which COF can be associated include other cemental lesions,[23] aneurysmal bone cyst[24] and Paget's disease.[25]

With the exception of the remarkably significant predisposition for females, COF affecting the Hong Kong Chinese exhibits clinical and radiological features consistent with those reported in other populations.

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Fibrous dysplasia in the jaws of a Hong-Kong population: radiographic presentation and systematic review

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Objective: To compare the radiographic presentation of fibrous dysplasia in the jaws of Hong Kong patients with the features reported in other populations.
Methods: The clinical records and radiographs were reviewed of seven patients with fibrous dysplasia whose diagnosis had been histopathologically confirmed. Published series of fibrous dysplasia were subjected to systematic review.
Results: The male:female ratio was 4:3: one woman was Indian in origin; the other six patients were ethnic Chinese. The females were on average older than the males. Three cases affected the mandible and four the maxilla. Five cases affected the right side and two the left. A swelling was the principle clinical manifestation. The lesions were generally large, affecting most or all of the hemimandible or hemimaxilla involved. All cases exhibited expansion and had ground glass opacification. The four cases affecting the maxilla reduced the lumen of the maxillary antrum. The systematic review was carried out on 104 individual cases derived from nine reports of which only 93 cases were accompanied by radiological details. Many of the reports were limited in their scope, particularly with regards to radiological features. Fibrous dysplasia is more frequent in the maxilla in Oriental populations. Swelling is the most frequent clinical finding and buccolinqual expansion the most frequent radiological finding.
Conclusion: The pattern of presentation of fibrous dysplasia in a Hong Kong population is broadly in agreement with reports from other populations.

Keywords: radiography, dental; fibrous dysplasia; jaw; jaw diseases

Introduction

Fibrous dysplasia affecting the jaws is an uncommon developmental anomaly. It may be divided into three categories; monostotic (74%), polyostotic (13%) and craniofacial (13%).[1] The last category, identified by Davis and Yardley,[2] appears to be confined to the face and jaws involving two or more bones. The specific cause of fibrous dysplasia is unknown, but a common theory for the monostotic form is that a nonspecific reaction to some disturbance induces an excessive proliferation of connective tissue[3] which is replaced by irregular bone trabeculae. These trabeculae increase in size and number as the lesion matures.[4]

Fibrous dysplasia is one of the group of fibrous-osseous lesions which also include cemento-osseous fibroma (COF), cementoblastoma and cemento-osseous dysplasia.[5] Although this group of lesions contains reactive lesions, harmatomas and neoplasms they cannot be distinguished on the basis of the histopathology which can only confirm their common fibro-osseous nature; the definitive diagnosis relies on the radiology. The importance of the radiology is especially highlighted in differentiating between fibrous dysplasia and COF; if the margin is well-defined then it is COF whereas if it is poorly defined it is fibrous dysplasia.[1] This distinction is important because COF is a benign neoplasm that can be treated by enucleation in most cases compared with fibrous dysplasia which is self-limiting[5] and may only need recontouring.[4]

It is generally held that the radiographic presentation of fibrous dysplasia varies according to the degree of maturation which determines the degree of opacification.[4] Although the most frequent description is 'ground-glass',[4] other patterns were reported by Waldron and Giansanti as 'smoky' and 'cloudy'[6] and

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by Obisesan and coworkers[7] as 'peau d'orange', 'whorled', or 'diffuse sclerosis' (which appears to be similar to or the same as 'ground glass').

The initial radiolucent stage of fibrous dysplasia may suggest central giant cell granuloma, traumatic bone cyst, aneurysmal bone cyst[4] and COF. The generally younger age of onset and its unilateral distribution allows fibrous dysplasia to be readily differentiated from Paget's disease which affects older patients and is frequently bilateral.

Over the past four decades there has been a considerable number of reports on fibrous dysplasia affecting the jaws but only eight reports applied the radiological test described above,[1,6–12] amounting to 97 individual cases. There was only one report of fibrous dysplasia affecting the jaws of an Oriental population; it was Korean.[8]

In this paper I report the clinical and radiological manifestations of seven cases of fibrous dysplasia affecting the jaws of a largely Chinese population and compare these features with the 97 reported in the literature.

Materials and methods

Hong Kong group

The review of the pathology records, between 1982 and 1990, of the Dental Hospital and School of the University of Hong Kong revealed seven patients with fibrous dysplasia, where the diagnosis had been histologically confirmed. Their clinical notes and radiographs were retrospectively reviewed. Each patient's ethnic origin, sex, age, clinical history and findings on examination and the differential or provisional diagnosis was obtained from the clinical records. Each lesion had been radiographed in two planes. Panoramic radiographs (Panelipse, GE, Milwaukee, USA) were available for all cases and were supplemented by skull views and intra-oral radiographs (periapical and/or occlusal) where appropriate. In order to diminish the effects of expectation bias, which is intrinsic to a retrospective review of cases, I first established the generally accepted radiological criteria for fibrous dysplasia from the literature (including standard texts, such as by Goaz and White[4]). The literature reviewed for this purpose concerned not only fibrous dysplasia but also COF. CT (Pace, General Electric, Hong Kong) was available in one case (Case 4): the window width and level were 2296 and 116 HU respectively.

The radiographs were viewed on a standard illuminated screen. The criterion used to determine the degree of definition of the boundary of the lesion was that established by Slootweg and Müller;[12] a lesion was considered to be well-demarcated when its radiodensity changed markedly within a distance of 1 mm when passing from the lesion to the surrounding bone. The influence of the lesion on adjacent structures, such as the teeth, the buccal and lingual cortices, lower border of the mandible and the maxillary antrum, was also recorded. The number of cases was too small for statistical analysis. The histopathology had been reviewed by the histopathologist who was prepared to review any case which was found to be inconsistent with the radiology.

Systematic review

The systematic review was undertaken by searching for the results of all studies which had addressed a similar research question: what are the clinical and radiological features of fibrous dysplasia of the jaws?

The reports summarised in this study were principally obtained from indexes such as Index Medicus and The Index of Dental Literature and the database Medline. The keywords sought were 'Fibrous Dysplasia', 'Cementomas' and 'Odontogenic Tumours'. In order to locate any recent publications not yet indexed, I reviewed the last 6 months of Current Contents/Life Sciences. The search of these indices and databases was supplemented by a hand search of English language journals on medical and dental radiology, otolaryngology, maxillofacial surgery and oral surgery. This strategy was further augmented by reference to the bibliographies of the literature in both the journals identified by the indexes, the database and textbooks. The reports were arrayed in chronological order. I did not attempt to include unpublished data in the search.

Papers for inclusion in this report were subjected to a checklist; they were excluded on the basis of the following criteria: (a) they considered fibrous dysplasia and the cemento-ossifying fibroma (or its alternative

Table 1 The sex, age and location of fibrous dysplaia in seven Hong Kong patients

Case no.	*Sex*	*Age (years)*	*Right* 8 7 6 5 4 3 2 1	*Left* 1 2 3 4 5 6 7 8
Mandible				
1[a]	F	10	Condyle < ——— > I	
2	M	16	Mandibular Foramen < —— > I	
3	F	21		I < ——— > Angle
Maxilla				
4	M	14	Retromolar < ——— > I	
5	M	18	Retromolar < ——— > I	
6	M	18		I < ——— > Retromolar
7[b]	F	33	Retromolar < ——— > I	

[a]Age at initial presentation and treatment, now 41 years. [b]Indian origin

Table 2 Summary of the clinical and radiological features of seven cases of fibrous dysplasia in Hong Kong patients

Case No.	*Signs and symptoms*	*Differential diagnosis*	*Radiological features*									
			Lucent	*Opacification Ground glass*	*Peau d'orange*	*Sclerosis*	*Definition of margin*	*Cortex thinned or absent*	*Expansion*	*Inferior border of Mandible Displaced*	*Thinned*	*Inferior dental canal Displaced?*	*Lamina dura intact?*
Mandible													
1	FD operated on when 10 & 25 years old. Staticnary for the last 15 years	FD	–	Yes[a]	–	Yes	Not defined	Yes	Yes	Yes	Yes	No	N/A
2	Ref, enlarged mancible	FD	–	Yes[a]	Yes	Yes	Not defined	Yes	Yes	Yes	Yes	Yes	No
3	Increased swelling for 5 years	FD	–	Yes[a]	–	–	Not defined	Yes	Yes	Yes	No	No	No
Maxilla									*Reduction of Antrum*				
4	Rt. maxilla swelling	FD	–	Yes[a]	–	–	Not defined	Yes	Yes		Yes		INA
5	Ref. rt. face swelling	FD	–	Yes[a]	–	–	Not defined	Yes	Yes		Yes		No
6	Extensive swelling l.. maxilla	FD	–	Yes[a]	–	–	Not defined	Yes	Yes		Yes		INA
7[b]	Extensive swelling rt. maxilla	FD	–	Yes[a]	–	–	Not defined	Yes	Yes		Yes		INA

INA, information not available; N/A, not applicable–affected jaw was edentulous; FD, fibrous dysplasea; [a]predominant pattern; [b]Indian origin

nomenclature) merely as points on the spectrum of the same disease or as its synonyms; (b) they failed to include radiology or histopathology in the diagnosis of their lesions; (c) they failed to disclose the radiological criteria used or used the wrong criteria; (d) their data had already been reported and included in the review; (e) they reported lesions that were derived from a discrete age group or a particular jaw and (f) they reported lesions that displayed a peculiar, even unique, feature/s. Because many of these criteria could only be determined by an in depth analysis of the whole paper it was crucial that the survey was confined to the English language journals.

Significance was assessed when $P<0.05$ ($X^2>3.84$) at one degree of freedom.

Results

Hong Kong group

The clinical and radiological details of the seven cases are set out in Tables 1 and 2. Three lesions were observed in the mandible and four in the maxilla. Five lesions affected the right side alone and two the left. The male:female ratio was 4:3 and the mean age was 18.6 (s.d. 7.2 years). Six patients were ethnic Chinese and one woman was of Indian origin (Case 7). The females were older than the males: (the male mean age was 16.5 (s.d. 1.9) years and the female mean was 21.3 (s.d. 11.5) years).

All cases presented with swelling. One patient (Case 1) had been surgically treated initially when she was 10 years old and again when she was 25.

Figure 1 (Case 2) Part of a panoramic radiograph displaying marked vertical expansion of the right side of the body of the mandible. The inferior dental canal has been displaced markedly downwards. Although the lesion exhibits a predominantly 'ground glass' pattern there are some linear trabeculae below the inferior dental canal and the region below the premolars is radiolucent. The lower border of the mandible is completely absent from the angle almost to the midline. The second and third molars have been displaced backward into the ramus

Opacification of the lesion was clearly apparent in all cases. Each of these lesions was unilateral and was so extensive that by the time it was radiographed it had affected almost the whole hemi-mandible or hemi-maxilla. The prevailing radiological feature was 'ground glass opacification, (Figure 1): 'peau d'orange' (Figure 2) and denser areas of sclerosis were also apparent.

The shape of the mandibular lesion was fusiform, whereas the maxillary lesions generally followed the shape of bone (Figure 3). All lesions had expanded the alveolar process buccolingually (Figure 3b). All three lesions affecting the posterior mandible had caused downward displacement of the inferior border of the mandible (Figures 1 and 4), whereas only one case was associated with downward displacement of the inferior dental canal (Figure 1). Case 1 had a fracture, exhibiting non-union, through the posterior body of the mandible (Figure 4).

All four maxillary lesions had displaced the floor of the maxillary antrum upwards, reducing it in size or, as seen in Case 4 obliterating it (Figure 3). The full extent of the lesion in Case 4 was only fully appreciated on CT (Figure 3b).

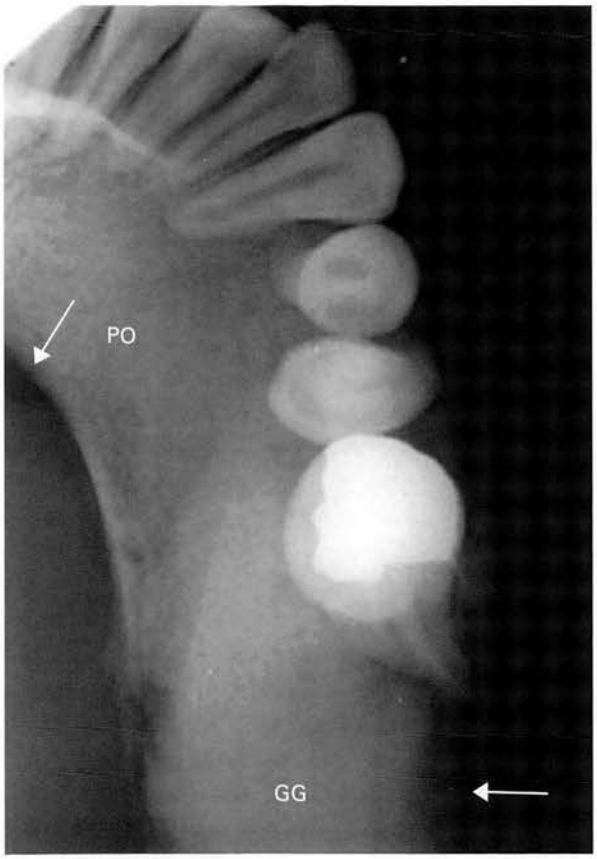

Figure 2 (Case 2) A true occlusal radiograph displays the variety of density and pattern seen in fibrous dysplasia, 'ground glass' (GG) posteriorly and 'peau d'orange' (PO) anteriorly. The cortex has been expanded and substantially thinned (arrows) not only posteriorly where the subjacent dysplastic tissue is more translucent, but also medially anteriorly. The roots of the premolars and first molar have been displaced buccally

In Case 2 both premolars and first molar were buccally displaced (Figure 2) and the second and third molars were displaced backward and upward into the ramus (Figure 1). The lamina dura was absent in the three cases where teeth were present in the dysplastic part of the mandible. No resorption of the teeth was observed in this study. The cortex of the affected sites was thinned and frequently absent both on plain films and CT bone windows.

The differential diagnosis was provided in all cases by the referring hospital clinicians and consisted only of fibrous dysplasia.

Systematic review

The summaries of the clinical findings, distribution by age and radiological features reported in the literature are displayed on Tables 3, 4 and 5 respectively. Females and the maxilla were more frequently affected (Table 3). The maxilla was significantly more frequently affected in Orientals ($X^2 = 6.3$); the greater frequency of females was not significant ($X^2 = 0.2$). Swelling was reported in 94% and pain in 14% of cases. The mean age at diagnosis was 25 years, although fibrous dysplasia was most frequently diagnosed in the second decade (45.7%; see Table 4).

Table 5 reveals that 93 of the 104 patients included some radiological details. The distribution of (−) ('information not given') and IIGs ('inadequate information given') reveals the extent of deficiency of the radiological description in many of those reports. Furthermore, in those instances in which entries had been made, it is clear that they were frequently incomplete.

There were over 36 'ground glass' (seven reports), four radiolucent (two reports), over two 'peau d'orange' (two reports), eight 'mottled' (two reports), one 'whorled' (one report), four 'smoky' (one report) and two 'cloudy' (one report); the six sclerotic cases where no pattern was specified were included under 'sclerotic' (three reports). For those cases for which details were available 91% were ovoid (or round in some cases), all displayed buccolingual expansion and all maxillary cases were associated with antral involvement. Forty-one per cent of 32 cases exhibited tooth displacement.

Discussion

The results for the Hong Kong population in this study will be discussed in relation to the clinical findings, age and radiology that emerged from the systematic review of the 104 cases. Although the mean age of 19 years in these patients was lower than that of the overall mean of 25 shown in Table 3, it is closer to the other reports in Table 4 where it can be seen that the lesion occurs most often in the second decade. Although one patient in the fifth decade in the present report (case 1) had remained static for the 15 years after surgery in the third decade does confirm the harmatomatous nature of this lesion, Waldron

considered that some cases of fibrous dysplasia were neoplastic.[13].

The predilection for males in this study differs from the majority of reports; Table 3 reveals a preponderance of females. Nevertheless, it would appear that the other Oriental population (Korean) did not differ from other groups in this respect. The report of fibrous dysplasia being initiated[14] or reactivated[15] during pregnancy suggests that female sex hormones may play a major role in the predilection of fibrous dysplasia of the jaws for females shown in Table 3. Furthermore, females with fibrous dysplasia were observed more frequently in the older decades (Table 4) but this was not significant.

The majority of lesions occurring in the jaws in the present study principally presented as a swelling which was reflected by the expansion of the affected bone seen on the radiographs. This finding is consistent with the systematic review in which clinically apparent swelling (Table 3) and radiographically apparent expansion (Table 5) were present in 94 and 100% of cases respectively. The expansion of the mandible involved not only the lingual and buccal plates but also the lower border.

Fibrous dysplasia affecting the maxilla almost always involves the antrum (Table 5) which it not only occasionally obliterates[4] but also displaces the orbital floor upwards; this was apparent in Case 4; maxillary lesion clearly encroaches upon the orbital cavity.

It is clear that CT was invaluable for the assessment of extensive lesions, especially those affecting the anatomically complex maxilla.[16,17] Furthermore, gross

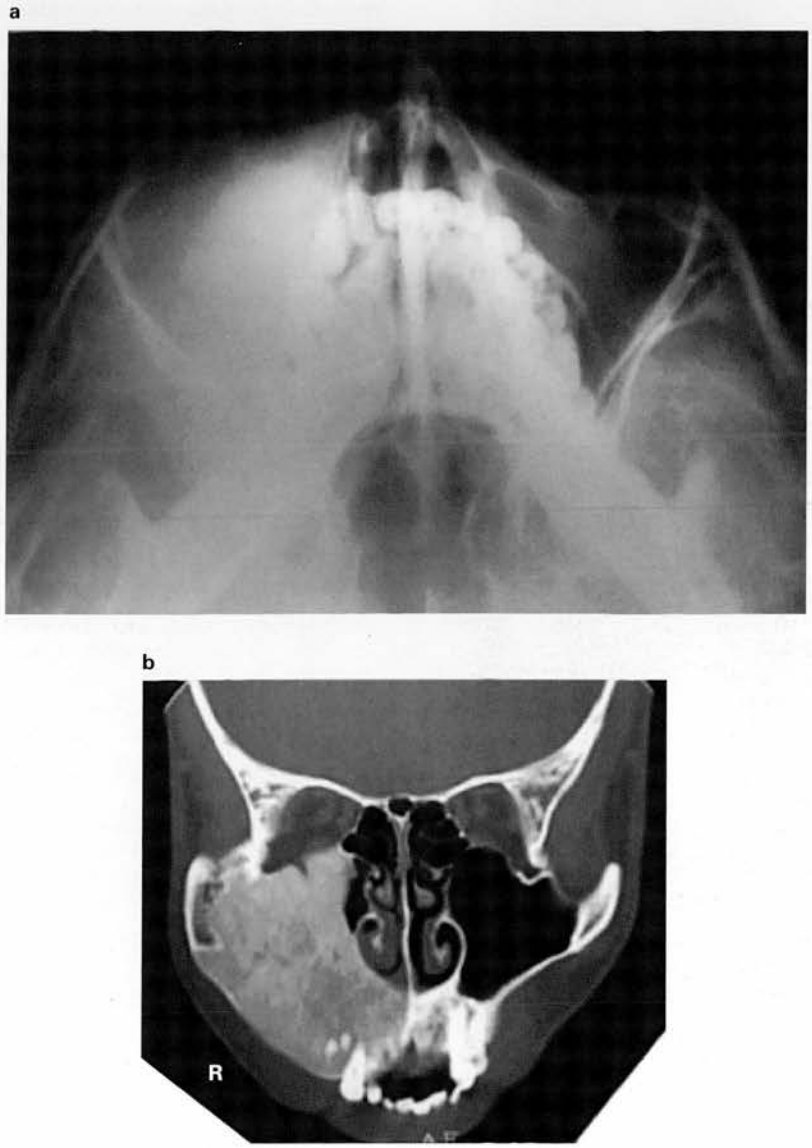

Figure 3 (a) (Case 4) An occipitomental projection exhibiting an extensive radiopacity with a 'ground-glass' appearance in the right maxillary antrum. Note the expansion of the right lateral and medial walls and the orbital floor. (b) (Case 4) A bone-window coronal CT scan confirming not only the substantial enlargement of the right side of the face but also almost complete obliteration of the lumen of the right maxillary antrum and inferior meatus. There is an upward displacement of part of the orbital floor. In many places the cortex is thin or absent. The alveolar process is also expanded buccolingually

sclerosis and thickening can create overlapping images which may impede adequate assessment by plain film radiography.[16]

The most common radiographic presentation of fibrous dysplasia in the present study was a poorly-defined, ovoid (fusiform-shaped) area of dysplastic bone that exhibited a 'ground glass' appearance; this was suggestive of a diagnosis of fibrous dysplasia.

Figure 4 (Case 1) Part of a panoramic radiograph showing significant enlargement of the ascending ramus and body of the right mandible. The proximal portion of the lesion has a 'ground glass' appearance whereas the distal portion shows patchy sclerosis. The fracture shows non-union. The body of the hyoid is superimposed upon the inferior aspect of the fracture

The degree of definition of the margins of the fibrous dysplasia is a very important diagnostic feature that allows the ready definition of fibrous dysplasia from other fibro-osseous lesions, in particular the COF; the former is poorly defined whereas the latter is well-defined.[1] The original reasoning behind this was developed by Sherman and others[18,19] and reaffirmed by Eversole *et al*;[1] diffuse lesions are dysplastic and well-defined lesions are benign neoplasms. The criterion which I used to determine definition was that of Slootweg and Müller;[12] its application confirmed the poorly defined nature of the dysplastic lesions in the present study in contrast to the generally well-defined neoplastic COFs in the same population.[20] Waldron and Giansanti[6] observed that the anterior border of maxillary lesions was well-defined. They dismissed this as being a radiographic artifact since neither the occlusal film showed it nor surgery substantiated it.

The bone pattern may vary not only between different films (for instance, 'ground glass' on screen film and 'peau d'orange' on direct intra-oral film),[21] but also between different parts of the same radiograph[6] (Figure 2). Both these features were observed in the present study. The variation in density within a radiograph may indicate that different areas of the lesion mature at different times, but Cooke did not

Table 3 A summary of nine series of fibrous dysplasia of the jaws totalling 104 cases in various populations

Author	*Population (race)*	*Number of cases*	*Male : Female*	*Age (years) mean (range)*	*Signs and symptoms* *Swelling (%)*	*Pain (%)*	*Maxilla : mandible*
Schmaman *et al*[9]	South African	5	–	–	–	–	4 : 1
Eversole *et al*[1]	US (9W : 3B)	12 [2]	7 : 5	27	–	–	6 : 9
Obwegeser *et al*[10] [a]	Swiss	6	2 : 4	23 (7–55)	100	–	3 : 3
Waldron and Giansanti[6]	US	22	11 : 11	27 (5–64)	100	–	13 : 9
Obisesean *et al*[7] [b]	Nigerian	7	–	–	–	–	–
Adekeye *et al*[11] [c]	NIgerian	3 [3]	1 : 2	19 (14–27)	100	0	2 : 1
Yoon *et al*[8]	Korean	31 (4)[d]	12 : 19	–	87	19	24 : 3[d]
Slootweg and Müller[12] [e]	Holland	11[2](2)[e]	4 : 7[e]	28	–	–	5 : 2[e]
Present	Hong Kong	7	4 : 3	19 (10–33)	100	0	4 : 3
Summary		104	41 (45%) : 51 (55%)	25[f]	94[g]	15[h]	61 (66%) : 31 (34%)

Because the authors frequently failed to provide specific M : F, age or Max : Mand ratio this Table records only the available information for those cases that affect the jaws. The number of polyostotic cases is given in ( ). The number of cases in [ ] brackets are craniofacial rather than polyostotic. IIG = inadequate information given. [a]Three cases were excluded; one (4 year old male) displayed obvious features suggestive of cherubism; two were polyostotic, one (7-year-old male) presented with well-defined lesions and the other (8-year-old male) with cherubism. [b]At least seven cases out of the 25 fulfilled the radiographic criterion. [c]Three out of five cases affected the jaws. [d]Four cases with multiple quadrants but no information if these cases are polyostotic or craniofacial forms. [e]Seven monostotic (3 : 4; mean age 31 years) and two craniofacial and two polyostotic (1 : 3; mean age 22 years); Max : Mand only available for monostotic. [f]Mean age of 61 cases; [g]Of 69 cases; [h]Of 41 cases

Table 4 The distribution of 81 cases of fibrous dysplasia by age (in decades). The values in parenthesis are male : female ratio

Deacde	*Eversole* et al[1]	*Obwegeser* et al[10]	*Waldron and Giansant*[6]	*Adekeye* et al[11]	*Yoon* et al[8]	*Hong Kong*	*Total*	*Percentage*
1st	0	2 (0 : 2)	1 (0 : 1)	0	0	0	3 (0 : 3)	3.7
2nd	6	2 (1 : 1)	9 (5 : 4)	3 (1 : 2)	12	5 (4 : 1)	37 (11 : 8)	45.7
3rd	0	0	3 (3 : 0)	0	12	1 (0 : 1)	16 (3 : 1)	19.8
4th	3	1 (1 : 0)	5 (1 : 4)	0	3	1 (0 : 1)	13 (2 : 5)	16.0
5th	3	0	2 (1 : 1)	0	2	0	7 (1 : 1)	8.6
6th	0	1 (0 : 1)	1 (0 : 1)	0	0	0	2 (0 : 2)	2.5
7th	0	0	1 (1 : 0)	0	2	0	3 (1 : 0)	3.7
Total	12	6 (2 : 4)	22 (11 : 11)	3 (1 : 2)	31	7 (4 : 3)	81 (18 : 20)	100

Table 5 Radiological features reported in 93 cases of fibrous dysplasia of the jaws

	Predominant radiodensity				*Shape of mandibular lesions*			*Expansion*			*Displaced tooth*[d]			
	Radiolucent	*Ground glass*	*Peau d'orange*	*Radiopaque Sclerotic*	*Other*[a]	*Ovoid*	*Multi-locular*	*Lower border expanded*	*Buccolingal Yes*	*Buccolingal No*	*Antral involvement Yes*	*Antral involvement No*	*Yes*	*No*
Schmaman *et al*[9]	0	5	0	0	0	–	–	–	–	–	–	–	–	–
Eversole *et al*[1]	3	6	0	0	6m	–	3	–	–	–	–	–	–	–
Obwegeser *et al*[10]	0	1	0	1	2c;1w	1	–	IIG	3	0	3	0	1	0
Waldron and Giansanti[6 b]	0		16[b]	0	4s	21	–	9	22	0	13	0	9	13
Obisesan *et al*[7]	0	4	2	0	0	7	0	–	–	–	–	–	–	–
Adekeye *et al*[11]	0	0	0	2	1	–	–	–	3	–	2	0	2	–
Yoon *et al*[8]	1	13	0	3	2m	–	–	–	–	–	–	–	–	–
Present	0	7	0	0	0	3	0	3	7	0	4	0	1	6
Summary	4	36	2	6	16	32	3	12	35	0	22	0	13	19
	5%		60 + 16[b] = 76 (95%)			91(%)	(9%)		(100%)	(0%)	(100%)	(0%)	(41%)	(59%)
			80			35			35		22		32	

IIG, imprecise information given. [a]Other: cloudy (c); smoky (s); whorled (w); mottled (m). [b]16 lesions exhibiting either 'ground glass' or 'peau d'orange': therefore there are more than the 23 'ground glass' and 2 'peau d'orange' specifically identified. [d]Some of the following tooth displacements may have been only identified on clinical examination

observe radiographic changes in comparable films over an interval of 10 years.[21]

A fracture was clearly demonstrated in Case 1 (Figure 4). Although this would appear to be the first reported case of a pathological fracture ocurring in fibrous dysplasia of the jaws, it is likely that the previous surgery would have contributed to it. Pathological fracture of the dysplastic jaws, while frequent in other bones affected by fibrous dysplasia,[22] has not been reported in the jaws.[23]

One case of tooth displacement was observed in the present study. Tooth displacement was also reported by Waldron and Giansanti[6] and Obisesan *et al*.[7] The lamina dura was absent in all three cases in the present series where assessment was possible. Petrikowski and her coworkers[24] suggested that the loss of lamina dura could be used as an ancillary diagnostic feature for fibrous dysplasia.

In the present study one of the three posterior mandibular lesions showed a marked downward displacement of the inferior dental canal. This finding disagrees with Petrikowski *et al*,[24] who did not find a single case of downward displacement. Indeed, they suggested that the upward displacement of the inferior dental canal was a unique characteristic of fibrous dysplasia.

The unilateral nature of fibrous dysplasia was apparent in all seven cases in the present study. The predilection for the right side observed in this largely Chinese population has already been noted for fibrous dysplasia affecting the maxilla in an American[6] population. Although this predilection may disappear as more cases are reported, it should be noted that this feature has been observed also in florid osseous dysplasia in this population.[25]

Because there is no spontaneous involution of fibrous dysplasia, the lesion has to be reduced by surgery[26] to improve the patient's appearance and function[16]; occasionally it may be employed to alleviate pain or ocular disturbances.[3] In the present series one mandibular lesion treated surgically had recurred once 16 years earlier, 15 years after the initial procedure.

Indices and databases do not record all relevant publications; Medline only indexed 25% of all medical publications that could be described as journals.[27] Furthermore, according to Greenhalgh 50% of the reports indexed in Medline have been misclassified.[28] Therefore, it is essential to follow-up the references in the literature identified by the indices and databases[29] and carry out a detailed hand-search of journals.[30] Exclusion of unpublished data from the search avoided the risk of inclusion of covert duplicate publications into the systemic review.[31]

Fibrous dysplasia affecting the jaws in this largely Chinese series of cases displayed features that were similar to those in almost all other reports in the systematic review. The radiology of these lesions contributed not only to the accuracy of the diagnosis but also to the definition of the extent of the lesion.

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Dentomaxillofacial Radiology (2003) 32, 141–149

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SYSTEMATIC REVIEW

Florid cemento-osseous dysplasia: a systematic review

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Objectives: To evaluate the principal features of florid cemento-osseous dysplasia (FCOD) by systematic review (SR), with particular regard to comparison of Oriental with non-Oriental populations, and of reports derived from pathology files with those from non-pathology sources.
Methods: All alternative names for FCOD were used as search terms for two electronic databases, namely Medline and "Web of Science". Only multiple forms of cemento-osseous dysplasia occurring in a series in the reporting authors' case load were considered.
Results: Medline produced more SR-identified reports. The search terms "Cementoma" and "Osseous Dysplasia" were the most effective for both databases. One hundred and fifty-eight cases of FCOD were observed in 17 series of patients reported in 16 SR-identified reports. Fifty-nine percent of cases were found in Blacks, 37% in Orientals and 3% in Caucasians. Ninety-seven percent were females. Fifty percent of cases in the SRs were observed incidentally. Pain was most frequent in those with presenting symptoms, and was significantly more frequent in the Oriental series. In two studies on the same Chinese community, those cases found incidentally on radiographs alone were significantly younger than those with symptoms in the pathology files.
Conclusion: The nomenclature for FCOD is extensive, but older and more general terms were more effective in recalling SR-identified reports. Cases in a report based on pathology files appear to be older than those in a report based on radiology alone files. With the exception of a higher prevalence of pain in Orientals, mainly Chinese, there did not appear to be any differences in presentation compared with that observed in Black communities.
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Introduction

Florid cemento-osseous dysplasia is a well recognized lesion predominantly affecting middle-to-old aged Black women. Once diagnosed, treatment is not generally necessary. The term florid cemento-osseous dysplasia (FCOD) has been proposed in the 2nd edition[1] of the World Health Organization's (WHO) "International histological classification of odontogenic tumours" to replace the 1st edition's "gigantiform cementoma".[2] FCOD is defined as "Lobulated masses of dense, highly mineralised, almost acellular cemento-osseous tissue typically occurring in several parts of the jaws...".[1] Although the 2nd edition essentially upheld the 1st edition's definition of FCOD, it modified the 1st edition's definition of periapical cemental dysplasia (PCD),[2] another cemento-osseous dysplasia (COD), which "mostly [affected] mandibular incisors" to "which may be adjacent to one another or in different parts of the jaws".[1] The problem with this is that it confuses the boundary between FCOD and PCD, if they are indeed two distinct lesions. The WHO definition only refers to the end-stage for FCOD, but considers the natural history of PCD including initial radiolucent and final "dense mineralized mass" stages. Furthermore, PCD need not be multiple, as the definition clearly recognises that PCD can affect single teeth. The sole point that appears to separate FCOD and PCD is that for PCD "Each periapical lesion is self-limiting, rarely exceeds 1 cm in diameter...".[1] By creating a separate category of "other cemento-osseous dysplasias" for those "lesions which share some of the features of periapical and/or florid cemento-osseous dysplasia, but do not have their characteristic clinicopathological patterns of presentation", the authors of the 2nd edition[1] accepted that further development in this area is required. Since the publication of the 2nd edition, two other types, which did exist prior to its publication, have become largely accepted. They are

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Waldron's "familial gigantiform cementoma"(FGC)[3] and his "localized fibro-osseous-cemental lesions",[4] renamed "focal COD".[5,6] The former predominantly affects more than any one individual of either gender and of any age of the proband's siblings or parents. It is frequently associated with excessive growth requiring surgery. Interestingly, Philipsen and Reichert[7] have not commented on these developments in their proposed amendments to the 2nd edition.

The 2nd edition's qualification that "Black persons are affected more commonly than Caucasians, and sometimes there is a familiar distribution"[1] cannot be considered immutable, as the occurrence of this lesion in Orientals was relatively unreported at the time of the 2nd edition. Indeed, their words "more commonly" and "sometimes" make it clear that this sentence is advisory rather than forming part of the definition.

This study considered only the multiple forms of COD that occurred in a series in the reporting authors' case load, thereby excluding case reports. These multiple forms should occur in two or more sextants and are therefore FCODs. The aim was to systematically review all reports that pertain to FCOD. The systematic review (SR) in this study addressed the questions "Do Chinese/Orientals have a different presentation of FCOD compared with non-Chinese/Oriental populations?" and "Do reports based on pathology files have a different presentation of FCOD compared with those based on non-pathology sources, such as radiology files?"

Material and methods

The search terms derived from alternative nomenclature for FCOD were used to interrogate two commonly used and independent electronic databases, namely Medline and ISI "Web of Science". Selection criteria were then applied to the output from the searches and a SR was performed on the surviving literature. The search terms used (Table 1) were synonyms for FCOD, PCD and COD in general; "Diffuse Sclerosing Osteomyelitis" is not a synonym *per se* for FCOD, but has been included because it contributes to the discussion. The only MeSH term relevant to the SR was "Cementoma". [Search terms in this report will be quoted in full, in parenthesis and with upper case initial letters, *e.g.* "Florid Cemento-Osseous Dysplasia".]

Medline contains medical articles from 1963 and is available free using the PubMed interface. The version of Web of Science used in this study goes back to 1945 and reviews a different selection of journals. It also has the "cited reference search" that prospectively identifies all reports within its database that have cited a particular report. The 23 search terms were derived from textbooks, periodical articles and both editions of the WHO's classification of odontogenic tumours.

There were two principal inclusion criteria for the SR: (a) the study should be consistent with the WHO definition of FCOD; and (b) the study should represent a complete collection of cases of FCOD occurring in the reporters' case load.

Consistency with the WHO definition

The study had to be consistent with at least the 1st edition[2] of the WHO's histological classification of odontogenic tumours. This edition described "Gigantiform Cementoma" as multiple, often symmetrical masses of cementum typically occurring in several parts of the jaws (derived from text and table). The word "often" was interpreted as advisory, but "multiple" and "typically" were essential to the definition. The 2nd edition's use of "sometimes" with reference to "familial" was only advisory and appeared to apply subsequently to "familial gigantiform cementoma" (FGC), a separate lesion with entirely different clinical manifestations and behaviour. Furthermore, hypercementosis was expressly excluded from the definition. Outside these core terms there remained scope for further qualification. Cystic change usually in the form of traumatic bone cyst (TBC) is now generally considered to be a concomitant lesion or manifestation of COD.

FCOD has been widely defined for the purpose of this study as multiple lesions occurring in more than one sextant. As the pattern of these multiple lesions should be observable on radiographs that are generally considered adequate for diagnosis, radiology-only studies without histopathological confirmation were admitted in order to determine whether there were any differences in presentation between pathology file and radiology-only reports.

Representation of a complete collection of cases of FCOD occurring in the reporters' case load

Reports were included only if they represented all the cases of FCOD that attended and were identified and recorded at their institutions. A selection of cases, such as case reports, were excluded.

The literature consistent with the above inclusion criteria was then subjected to more specific exclusion criteria: "Criterion A" excluded reports whose data have already been reported and included in the review; "Criterion B" excluded reports of lesions in association with other abnormalities; "Criterion C" excluded reports in which it is clear that the whole of the jaws had not been conventionally radiographed; and "Criterion D" excluded reports in which it was impossible to determine and/or identify the number of FCODs, in contrast to PCD, and more particularly solitary or "focal" COD.

To achieve the maximum inclusion of reports, those reports considered for exclusion under Criteria C and D were researched for earlier and perhaps fuller reports in theses or local journals that may provide more essential details that could salvage them. Because the diagnosis of FCOD is dependent on radiography of the whole jaws, reports (Criterion C) that cannot provide radiographic details for all their cases can nevertheless be partially salvaged and included in the SR if the cases that have radiographs can be readily identified.

Medline and Web of Science were interrogated by the search terms (see Table 1), and this was supplemented by a hand search of journals on medical and dental radiology,

Table 1 Search terms for two electronic databases, Medline (Med) and Web of Science (WoS) used in the systematic review (SR)

	Total No. of reports		*No. of reports included in SR*		*Recall (%)*[a]		*Precision (%)*[b]		*Bibliography of reports included in SR*	
Search terms	*Med*	*WoS*	*Med*	*WoS*	*Med*	*WoS*	*Med*	*WoS*	*Med*	*WoS*
(a) Florid Osseous Dysplasia	42	21	5	5	31.2	31.2	11.9	23.8	21,27,38–40	20,21,27,34,38
(b) Florid Ossifying Dysplasia	8	0	0	0	0	0	0	0	—	—
(c) Florid Cemento-Osseous Dysplasia	19	11	2	0	12.5	0	10.5	0	39,40	—
(d) Florid Cemento-Ossifying Dysplasia	2	0	0	0	0	0	0	0	—	—
(e) Gigantiform Cementoma	25	25	6	5	37.5	31.2	24.0	20.0	20,27,34,35,41,42	20,21,28,35,38
(f) Familial Multiple Cementomas	2	0	0	0	0	0	0	0	—	—
(g) Periapical Cemental Dysplasia	40	13	5	1	31.2	6.2	12.5	7.7	31,33,39,41,42	41
(h) Periapical Cemento-Osseous Dysplasia	14	2	1	0	6.2	0	7.1	0	39	—
(i) Periapical Osseous Dysplasia	25	0	4	0	25.0	0	16.0	0	31,37,39,42	—
(j) Periapical Fibrous Dysplasia	26	1	3	0	18.8	0	11.5	0	38,41,42	—
(k) Benign Periapical Fibroma	10	0	2	0	12.5	0	20.0	0	31,41	—
(l) Cemento-Osseous Dysplasia	30	23	2	0	12.5	0	6.7	0	39,40	—
(m) Cemento-Ossifying Dysplasia	11	0	1	0	6.2	0	9.1	0	42	—
(n) Multiple Enostosis	8	2	1	1	6.2	6.2	12.5	50.0	28	28
(o) Multiple Endostosis	0	0	0	0	0	0	0	0	—	—
(p) Sclerosing Osteitis	12	5	2	1	12.5	6.2	16.7	20.0	28,34	28
(q) Sclerosing Osteomyelitis	162	124	4	1	25.0	6.2	2.5	0.8	28,34,37,40	28
(r) Chronic Sclerosing Osteomyelitis	108	38	2	1	12.5	6.2	1.8	2.6	28,37	28
(s) Diffuse Sclerosing Osteomyelitis	54	56	2	0	12.5	0	3.7	0	37,40	—
(t) Periapical Osteopetrosis	4	1	0	0	0	0	0	0	—	—
(u) Benign Fibro-Osseous Lesions of Periodontal Ligament Origin	5	1	2	0	12.5	0	40.0	0	28,31	—
(v) Cementoma	243	48	7	6	43.8	37.5	2.9	12.5	20,28,34,35,40–42	20,21,28,32,35,41
(w) Osseous Dysplasia	418	118	9	4	56.2	25.0	2.2	3.4	20,27,28,31,34,36,40–42	20,21,27,28,34

[a]Recall was expressed as SR-identified reports for that search term for that database as a percentage of the total number of SR-identified reports, which is 16
[b]Precision was expressed as SR-identified reports as a percentage of the total number of reports for that search term for that database
Both databases were last interrogated by all search terms on the 31 January 2003

otolaryngology, maxillofacial surgery, oral surgery and oral pathology. This strategy was further augmented by reference to the bibliographies (or citation lists) of all reports identified by the databases or hand searching. On the occasion where uncertainty arose that could result in the report's exclusion from the SR, the report's authors were contacted for clarification.

"Recall" and "precision" for each search term and database were defined and displayed in Table 1 as percentages. Recall was expressed in SR-identified reports for that search term for that database as a percentage of the total number of SR-identified reports. Precision was expressed in SR-identified reports as a percentage of the total number of reports for that search term for that database.

The "number of FCODs per hospital per year" reflected the number of hospitals contributing to the report and the number of years from which the reported series was derived.[8]

The jaws were further divided into posterior (molar and premolar) and anterior (incisors and canines) sextants. Although the demarcation point between these areas was infrequently expressed, it was taken to occur at a vertical line just distal to the distal surface of the canine.

Significant differences in frequencies were tested by the χ^2 test with $P < 0.05$ ($\chi^2 \geq 3.84$) at one degree of freedom. Significant differences in age were tested by the Student t-test with $P < 0.05$.

Results

The search terms and both databases identified all but one report that may be relevant to the SR; Wu and Chan's[9] report was only identified by reviewing bibliography lists. The Web of Science's "cited reference search" did not identify any SR reports in addition to those already identified by the search terms and review of the bibliography. Table 1 displays each search term, the total number of reports, the recall and precision for both databases, and the identity of those reports.

Many of the reports that initially appeared to be relevant to the SR were rejected because they were actually single case reports, review articles or, in the case of those identified under cementoma, concerned with other cemental lesions. Zegarelli et al[10] did not fully understand that cementifying fibroma (or fibrocementoma as they called it), cementoblastoma and COD are separate lesions. Panders and Hadders[11] included a number of cases that were not FCOD; this report will be discussed later. Other reports were rejected because they clearly were not derived from a complete collection of cases of FCODs occurring in the reporters' case load. Both Hamner et al[12] and Bhaskar's[13] reports were based (partly and wholly, respectively) on secondary referrals from military communities and were therefore not representative of a hospital-based patient community. Schneider and Mesa's report[14] was rejected because it was likely that it

represented two selected cases of FCOD rather than a presentation of all cases. Ariji et al's[15] report with a "special emphasis on computed tomography" was excluded because their seven cases were "selected".

Altogether there were 28 reports that appeared to comply with the inclusion criteria. Three sets of reports were considered under Criterion A. Two of the reports of Kawai et al overlapped (1952–1972[16] and 1969–1997[17]), but it was unlikely that 3 years of overlap would result in significant double reporting. Laband and Leacock's two reports[18,19] double reported the same series, therefore one would have to be excluded. MacDonald-Jankowski[20,21] also had some overlap between reports, but the two double-reported Chinese cases were identified and removed from the earlier report[20] in the SR. The final decision on the inclusiveness of the double reports of Kawai et al[16,17] and Laband and Leacock[18,19] was deferred to Criterion D.

Six reports were considered under Criterion B. Higuchi et al's report[22] was concerned with only those CODs associated with cysts in the mandible. The report by Abdelsayad et al[23] appeared to be based on FGC. Yoon et al's report[24] was excluded, as the description in each of the three cases of "gigantiform cementoma" was strongly suggestive of FGC. The reports by Regezi et al[25] and by Fontaine[26] were excluded because the lesions they reported were essentially focal COD or PCD. Melrose et al[27] included 14 cases that combined FCOD with TBCs. Their report was rescued and included in the SR because their series represented all the cases of FCOD with radiographs.

Two reports were considered under Criterion C. Wu and Chan's report[9] made no reference to radiographs and was excluded. Waldron et al[28] had only 14 cases with full radiographs out of 38 cases in their pathology file. As these 14 cases could be identified, the report was partially rescued and included in the SR.

Of the seven reports considered under Criterion D, six[16–19,29,30] were excluded as they failed to provide sufficient information to determine whether their lesions were FCOD or other types of CODs. Neville and Albenesius' report[31] was rescued and included in the SR because the 9 non FCODs out of their 29 cases were readily identifiable and excluded.

Of the 23 search terms used in Table 1, "Osseous Dysplasia" recalled the most SR-identified reports overall for Medline, but it had a low precision, which for Medline and Web of Science was 2.2 and 3.4, respectively. "Gigantiform Cementoma" had the highest precision for both databases.

A total of 16 reports survived the selection criteria and were accepted for the SR.[20,21,27,28,31–42] The details that they reveal are set out in Table 2. Two of those reports[20,31] were largely derived from non-biopsy sources. Of the reports included in the SR, Medline recalled seven reports[31,33,36,37,39,40,42] that were not recalled by Web of Science, whereas the latter recalled one report[32] not found in the former. Although this last report[32] was an abstract, it was published in a journal that Medline indexes. Nine search terms produced reports that were included in the SR for both databases. Medline provided SR-identified reports for nine search terms for which none were given by the Web of Science. Waldron et al's report[28] was the most cited, seven times each in Medline and the Web of Science.

In Table 2, the percentage of reports with details available varied greatly from 90% (142 cases) for gender to 59% (93 cases) for the presence or absence of pain in the 158 cases of FCOD observed in 17 series of patients reported in 16 reports.[20,21,27,28,31–42] Ninety-three (59%), 58 (37%) and 5 (3%) cases occurred in Blacks,[20,27,28,31,35,37,38,40,41], Orientals[20,21,27,32,33,34,39,42] and Caucasians (including three Indians),[28,34,36] respectively; the race was unknown in 2 cases.[27,40] The specific ethnic origin of the Orientals was clear in seven reports; three in Japan,[33,39,42] two in China,[20,21] and one report each for Singapore[34] and Korea.[32] Ninety-seven percent of the 142 cases that identified gender were female.

The mean age for 101 cases was 49 years. Although a mean age of 47 years was observed in three[20,33,34] of four Oriental series, the oldest mean age in the SR was for the Hong Kong Chinese series derived from histopathological files.[21] This was significantly older than the radiology-only series[20] for the same dental hospital patient community over a similar period ($t = 3.06$; 23 df; $0.01 > P > 0.001$). As reported by Neville and Albenesius,[31] the only other report that was based on radiology only diagnosis did not include a mean age, so observation of a similar phenomenon between comparable non-Oriental communities was not possible.

Half of 105 cases were discovered incidentally to investigation of a separate complaint. Pain, swelling and pus discharge/fistula were the symptoms in 52%, 31% and 18%, respectively. Although the frequency of FCOD found as an incidental finding or associated with swelling in the Orientals (largely Chinese) was not significantly different to that in non-Orientals (largely Blacks), the frequency of those presenting with pain was significantly higher in Orientals ($\chi^2 = 5.17$; $0.05 > P > 0.01$).

The mandible was involved in all and the maxilla in two-thirds of 97 cases. The frequency with which anterior and posterior areas were affected were 99%, 73%, 64% and 36% for the posterior mandible, posterior maxilla, anterior mandible and anterior maxilla, respectively. There was no significant difference between Oriental and other series with regards to the frequency that the maxilla or the anterior areas of the maxilla and mandible were affected.

Symmetry with regards to the sextants affected, rather than mirror image symmetry *per se*, was an important feature of FCOD whenever assessable. Symmetry was assessable in three reports and appeared to be greatest in the Chinese series, although in the histopathology-based report,[21] five lesions were completely unilateral in distribution. The ratio of the symmetrical maxillary to mandibular lesions was greater in one of the radiology-only reports.[20]

Discussion

In this study, the Medline database produced more useful reports than the Web of Science. As a central aim of a SR is to "systematically search... the world literature on a specific issue",[43] then a literature search by the Web of Science should be supplemented by a medical database such as Medline.

Generally, searches are a combination of MeSH (in Medline) and free-text search terms. The only relevant MeSH term was "Cementoma", first used as such in 1971. Although its definition in its "scope note" would not be inconsistent with that of "Cementoma" in the 1st edition of the WHO's classification of odontogenic tumours,[2] it did not include any of the WHO's subclassification of "cemental" lesions as entry terms (alternative nomenclature or subclassified lesions). Furthermore, when "Cementoma" was used as a search term in a free-text search it did not identify any useful references not identified by other search terms. This both highlighted the limitations of the current (2003) MeSH[44] in some areas of health care such as dentistry and radiology and the importance of free-text searching. The latter was enhanced if the terms appear in the title or abstract of papers submitted for indexing, because free-text searching was an automatic direct electronic search of all titles and abstracts in the database. The report by Wu and Chan[9] was not picked up because none of the search terms appeared in either their report's title or abstract.

The most effective search terms in terms of both recall and precision were "Florid Osseous Dysplasia" and "Gigantiform Cementoma". Although recall and precision are central properties of database searching, recall generally takes precedence, particularly in SRs in which the principal aim is to acquire the largest number of relevant papers. Although it was not unexpected that the most non-specific terms such as "Cementoma" and "Osseous Dysplasia" would have the highest recalls, certainly for Medline, it was unexpected that "Osseous Dysplasia" would be so effective, as it has not been used with respect to FCOD for decades. Therefore, as it is not possible to determine the efficiency of a search term in advance, the use of a wide range of nomenclature as search terms was justified.

Over time, as it became clear that conditions labelled "Chronic Sclerosing Osteomyelitis" were not associated with infection, leading to the development of "Cementoma" and "Benign Periapical Fibroma", there were those, such as Robinson,[45] who still proposed a reactive cause for these lesions, calling this lesion "Osseous Dysplasia". Waldron et al[28] advocated a periodontal ligament origin for this group of lesions because this class of lesion was generally confined to the alveolus and contained a histopathological appearance similar to that seen in the normal periodontal ligament. This concept is still generally applied today.[46]

Although Waldron considered that the majority of cases called "Chronic Sclerosing Osteomyelitis" were "Florid Osseous Dysplasia" (FOD),[4] Panders and Hadders[11] used "Chronic Sclerosing Osteomyelitis" in relation to cases that were clearly similar to Groot et al's "Diffuse Sclerosing Osteomyelitis", differing markedly from "Florid Osseous Dysplasia".[38] The former affected the basal process of the mandible in addition to the alveolar process, to which the latter was largely confined. SR reports identified by "Diffuse Sclerosing Osteomyelitis" included this term in the title[38] or abstract[33,40] as a lesion other than FCOD. "Chronic Sclerosing Osteomyelitis" and the more general "Sclerosing Osteomyelitis" identified many reports but very few SR-identified reports. "Enostosis" is now used as a synonym for "bone islands" that do not need treatment.[47]

WHO's 2nd edition terminology of FCOD and COD published in 1992 has not been consistently applied in the subsequent period.[1] Not only has the older "Florid Osseous Dysplasia" and even the almost obselete "Gigantiform Cememtoma" recalled more SR-identified reports on both databases, the latter identified two published in the last 2 years; these were not identified by the search term "Florid Cemento-Osseous Dysplasia". Although this can be expected as older terms will be more familiar, another reason could be that many authors may have considered the hyphenated "Cemento-Osseous" unnecessary, for which they have some justification. The term "Cemento-Osseous Dysplasia" is a histopathological term rather than a clinical or radiological term, yet diagnosis of FCOD is decided by clinical and radiographic investigation, its histopathology being similar to the two other fibro-osseous lesions (FOLs), cemento-ossifying fibroma and fibrous dysplasia. All three FOLs are characterised by replacement of bone by a benign connective tissue matrix, the matrix displaying varying degrees of mineralization in the form of woven bone or cementum-like round basophilic acellular intensely basophilic structures.[48] Therefore, Waldron wrote "In absence of good clinical and radiologic information a pathologist can only state that a given biopsy is consistent with a FOL. With adequate clinical and radiologic information most lesions can be assigned with reasonable certainty into one of several categories."[49]

Even before WHO's 2nd edition expanded its definition of PCD to include cases with lesions in posterior areas, it had already been used as a synonym for FCOD. Of the seven SR-identified reports, two used PCD to describe lesions that were consistent with FCOD,[31,33] and one mentioned PCD in the abstract but FCOD in the body of the text.[39]

Although the SR has shown that identification and application of the varied nomenclature to FCOD has been valuable for recalling reports from databases, it cannot do more than indicate which terms are most useful for such a purpose. Nevertheless, it is clear from the titles and abstracts of recent papers that some of the terms such as "Florid Osseous Dysplasia" that were in vogue before the recommendations of the WHO's 2nd edition are still being used. The continued use of many of those should not cause confusion, provided that they have not already become associated with other specific lesions, such as "Periapical Cemental Dysplasia" and its variant names, "Sclerosing Osteitis" and "Sclerosing Osteomyelitis". Nevertheless, some care is needed with the other WHO's 2nd edition

Table 2 Analysis of 17 reported series of florid cemento-osseous dysplasia (FCOD) (16 reports) accepted for the systematic review

Authors (date)	National and/or ethnic origin (No. of hospitals (H) and number of cities (C))	Period covered	Number of FCOD (No. per hospital per year)	Sex		Mean age (range) (years)	Presenting signs and symptoms directly arising from FCOD lesions			Site		Histopathology	Miscellaneous comments	Total number of citations per database	
										Mandible	Maxilla				
				M	F		Swelling	Pain	Other[c]	Ant. Post.	Ant. Post.			Medline	Web of Science
Waldron (1975)	US (12B;2W) (1H:1C)	17 years	14 (0.82)	0	14	—(34–67)	4	8	3 incidental 5 discharge pus	IIG	IIG	38 Only14 had full radiography		7	7
Melrose (1976)	US (32B;1O,1?) (1H:1C)	?	34	1	33	42 (26–59)	16	9	23 incidental	32 (34) 34	22 (24) 22	48 Only 34 included full radiograph of both jaws	7 max. and 20 mand. had symmetrical distribution	3	2
Neville (1986)	US (20B) (1H:1C)	4 years	20 (5.0)	0	20	—(21>80)	ING	ING	ING	IIG	IIG	8	Some of 9 excluded may be PCD. 8 biopsied	5	0
Kim (1987)	Korean (1H:1C)	20 years	1 (0.05)	ING		ING	ING	ING	ING	ING	ING	All 50 cemental lesions	3 cases of PCD in anterior mandible	0	1
Tanaka (1987)	Japanese (1H:1C)	?	3	0	3	47 (34–65)	0	0	3 incidental	2 (3) 3	1 (3) 3	3	Called PCD	1	0
Loh (1989)	Singaporean (8 Chin;1 In) (1H:1C)	31 years	9 (0.29)	0	9	47 (37–59)	4	9	9 discharge pus ± sequest NO numb 0 incidental	9	5	9	All affected jaws affected bilateral Mainly premolars	5	2
Thompson (1989)	South African (8B) (1H:1C)	20 years	8 (0.4)	0	8	56 (39–74)	IIG	IIG	IIG	2 (8) 8	0 (6) 6	8	9 out of 28 cases had symptoms	2	2
Swaroop (1990)	Indian (1H:1C)	18 years	2 (0.1)	ING		ING	ING	ING	ING	ING	ING	2		1	0
Saini (1991)	Saudi Blacks	?	4	0	4	43 (38–48)	1	ING	3 incidental	IIG	IIG	4	Poor quality figures	4	0
MacDonald (1992)	British (6B) (1H:1C)	2 years	6 (3.0)	0	6	54 (37–67)	0	0	6 incidental	4 (6) 6	2 (6) 6	Radiographs only	5 max. and 5 mand. had symmetrical distribution	3	4
MacDonald (1992)	Chinese (1H:1C)	10 years	8[a] (0.8)	0	8	47 (28–65)[a]	1	ING	7 incidental	6 (8) 7	3 (5) 5	Radiographs only	[a]2 other cases included in 1996 5 max. and 7 mand. had symmetrical distribution	3	4
Groot (1996)	Dutch (5B) (1H:1C)	?	5	0	5	53 (33–66)	3	5	4 fistula 0 incidental	0 (5) 5	0 (3) 3	IIG		2	2
MacDonald (1996)	Chinese (1H:1C)	10 years	17 (1.7)	0	17	62 (43–83)	4	11	5 incidental 1 pus discharge	7 (17) 17	4 (12) 12	17	5 max. and 11 mand. had symmetrical distribution	1	4
Miyamoto (1996)	Japanese (1H:1C)	20 years	13 (0.6)	IIG		IIG	ING	ING	ING	IIG	IIG	13	42 multiple lesion cases	6	0
Lahbabi (1998)	French (4B:1?) (1H:1C)	?	5	1	4	46 (33–64)	0	3	2 incidental	3 (5) 5	0 (1) 1	5 pans and 1 CT	Text and figures Not so clear on maxillary lesions	7	0
Ogunsalu (2001)	Jamaican (2H:2C)	15 years	2 (0.13)	0	2	48 (47–49)	ING	ING	ING	0 (2) 2	0	2	Excluded 1 GC — had only 1 lesion Also had 1 PCD	6	2

Table 2 (*continued*)

Authors (date)	*National and/or ethnic origin (No. of hospitals (H) and number of cities (C))*	*Period covered*	*Number of FCOD (No. per hospital per year)*	*Sex*		*Mean age (range) (years)*	*Presenting signs and symptoms directly arising from FCOD lesions*			*Site*			*Miscellaneous comments*	*Total number of citations per database*	
				M	*F*		*Swelling*	*Pain*	*Other[c]*	*Mandible*	*Maxilla*	*Histopathology*		*Medline*	*Web of Science*
										Ant. Post.	*Ant. Post.*				
Matsuzaka (2002)	Japanese (1H:1C)	35 years	7 (0.2)	2	5	IIG (30s—60s)	ING	ING	ING	IIG	IIG	7		7	0
Synthesis of all 16 reports[b] Mean						49 (21—83)									
Total number of FCOD cases		—	158	4	138		33/105 (31%)	45/93 (48%)	Incidental 52/105 (50%)	97/97 (100%)	65/97 (67%)				
Number of reported series (% of total of 17 series)			(12) (70%)	14 (82%)		11 (13) 65% (76%)	10 (59%)	7 (41%)	Incidental 10 (59%)	10 (59%)	10 (59%)				

[a]Two patients (Cases 9 and 10) were deleted from the 1992 series because they appear also in the 1996 series
[b]MacDonald-Jankowski (1992) reports two series, in Britain and in Hong Kong
[c]Also, pus discharge/fistula was 19/105. Although these were recorded in only 4 reports (25%), it is unlikely that their presence would have gone unrecorded if observed in the other 6 reports recording swellings; hence their presence was likely to have been considered in 105 cases
B, Black; W, White; O, Oriental; Chin, Chinese; In, Indian
max., maxillary; mand., mandibular; PCD, periapical cemental dysplasia; GC, gigantiform cementoma
IIG, inadequate information given; ING, information not given
pans, dental panoramic radiograph

FCOD synonym "Familial Multiple Cementomas".[1] This term recalled two reports of FGC, which has a different clinical presentation and prognosis.[3] Most cases of FGC have been reported in Caucasian kindreds, affecting all age groups of both genders equally. Also, the behaviour of many of the lesions are more akin to neoplasia, exhibiting progressive growth and necessitating surgery, which was otherwise contraindicated for the largely asymptomatic conventional form.

Stypulkowska's report[50] on 40 years coverage of oral tumours in a European community, which clearly considered FCOD, did not reveal a single case of FCOD, supporting the outcome of the SR that FCOD occurs more frequently in Blacks and Orientals than in Caucasians.

The percentages of details reported by the SR-identified reports compared favourably with other recent SRs.[8,51]

Although series of FCOD in Oriental communities are just as frequently reported as those in Black communities, the former's very low "number of FCOD cases per hospital per year" values in comparison with those of the latter's would indicate that the frequency of FCOD in Orientals may be lower than that experienced in Blacks. This phenomenon was more clearly seen in a report in which diagnosis was primarily radiological; the "number of FCOD per hospital per year" in MacDonald-Jankowski's British[20] Black series were particularly high in comparison with MacDonald-Jankowski's Chinese[20] series. The "number of FCOD per hospital per year" in the last series was half that observed in the same author's Chinese pathology file based report.[21] This can be explained by reports derived from pathology files being dependent upon the presence of clear indications for the surgery that is required to produce the pathological specimen. Such indications may only be forthcoming in a fraction of cases, as most may be symptom-free. Nevertheless, it is those symptomatic cases that compel the patient to seek treatment and ultimately appear in the pathology file. Some support for this contention was revealed in the SR. MacDonald-Jankowski's pathology file based report[21] was associated with symptoms. This series not only had the oldest mean age, but it is significantly older in comparison with the series from the radiology-only report[20] in the same community, in which nearly all FCODs were observed as symptom-free and incidental findings on radiographs taken to investigate other complaints. An important finding in the pathology file based Chinese report[21] was a significant association between edentulous areas and COD lesions, which could contribute a secondary infection and therefore symptoms. Loh and Yeo's report[34] most clearly displays the association between pain and discharge of pus and sequestrae formation. Furthermore, Waldron et al[28] claimed that most of their symptomatic cases had been "edentulous in the affected areas for many years"; all their 10 biopsies from edentulous sites had symptoms, whereas the four from dentate areas had none. Therefore, a significantly higher prevalence of pain in Oriental, mainly Chinese, reports may reflect this association between lesions in edentulous areas, otherwise the essential character of FCOD is to remain symptom-free unless secondarily infected.

Symmetry of distribution was an important observation. In the radiology-only report, it appeared that symmetry of distribution within both the maxilla and the mandible was a feature of the Hong Kong Chinese,[20] but when compared with the pathology file based report[21] on patients from this community this feature is less evident. The ratio of symmetry of maxillary lesions to mandibular lesions is also greater in the radiology-only report, whereas the Hong Kong pathology file based report[21] was comparable with the lower symmetry reported by Melrose et al,[27] which was also pathology file based. Furthermore, in the Hong Kong pathology file based report,[21] the unilateral, therefore asymmetrical, cases were on average younger than the bilateral cases. This unilateral presentation in younger patients may represent a transition stage to the classical bilateral distribution of the more mature lesion.

In conclusion, the mean age of a particular community may depend on whether it was a pathology-based or a radiology-based study, as symptoms-free lesions observed as incidental findings on radiographs were younger than those with presenting symptoms. Other than a significantly higher prevalence of pain in Orientals, particularly the Chinese, there did not appear to be other differences in presentation between the populations reviewed. As the maturation progress of FCOD has not been established, a longitudinal review of FCOD cases could determine their progress and sequelae, particularly with regard to edentulous areas. A better understanding of these could enhance dental management of increasingly ageing populations, particularly in the West (where the majority of reports regarding Blacks originate from) and in the Hong Kong Special Administrative Region of the People's Republic of China.

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SYSTEMATIC REVIEW

Multiple idiopathic cervical root resorption: systematic review and report of four cases

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Objectives: The objectives of this study were to report four cases of multiple idiopathic cervical root resorption and to systematically review the literature on this condition.
Methods: The clinical and radiographic findings and the medical/dental histories of four patients who presented with multiple idiopathic cervical root resorption were recorded. Additionally, 10 references from the literature that reported on 14 patients were reviewed.
Results: Multiple idiopathic cervical root resorption was an incidental finding on routine clinical and radiographic examination. There appeared to be no correlation between this type of resorption and any medical/dental finding. Radiographically, multiple idiopathic cervical root resorption was found to begin at the cemento-enamel junction and then either progress to involve the entire cervical region or, at some point, spontaneously arrest. Those cases that progressed to involve the entire cervical region required extraction. The number of teeth that demonstrated this condition ranged from 5 to 24 per patient. More teeth became involved as the condition was followed in time. There was no detectable frequency of occurrence for any particular dental region or tooth among the involved teeth. Of a total of 18 patients, 13 were females whose ages ranged from 7 years to 68 years. Ten of the 18 patients were Caucasian.
Conclusions: Multiple idiopathic cervical root resorption was found most frequently associated with younger females. This condition appeared to be of unknown aetiology and uncertain natural history.
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Keywords: cervical; tooth resorption; root resorption, multiple; idiopathic

Introduction

The aetiology of both idiopathic internal and external root resorption remains elusive. It may occur spontaneously, in the absence of either local or systemic factors. Idiopathic external root resorption has been found to be an infrequent phenomenon that affects either or both apical and cervical regions of one or several teeth, but most commonly occuring in the apical region. It is relatively rare to find idiopathic resorption associated with the cervical areas of the tooth and even more uncommon for the condition to involve multiple teeth.

The first reported case of idiopathic cervical root resorption was by Mueller and Rony[1] in 1930. Recently, systematic review has become increasingly important in current evidence-based research.[2–5] The goal of a systematic review is to minimize both bias and error, serving as an aid to clinical reasoning. The aim of this report was to describe the history, clinical findings and radiographic appearance of four unreported cases of multiple idiopathic cervical root resorption and to undertake a systematic literature review of this condition.

Materials and methods

Criteria for inclusion in this report were (1) patients with no systemic or local factors that may have contributed to root resorption, (2) resorption originating at the cemento-enamel junction of teeth and (3) resorption involving more than three teeth in the dentition.

A systematic review was performed by a search of Ovid databases (Copyright 2000–2002, Version 5.1.0; Ovid

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REVIEW

Fibro-osseous lesions of the face and jaws

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Odontogenic tumours; Cementoma; Fibrous dysplasia; Bone; Jaws; Radiology

Maxillofacial fibro-osseous lesions (FOL) consists of lesions that differ, with the exception of fibrous dysplasia, to those found in the rest of the skeleton. FOLs of the face and jaws are cemento-ossifying dysplasia, fibrous dysplasia and cemento-ossifying fibroma. Radiology is central to their diagnosis because the pathology for all FOLs is similar, although they range widely in behaviour, from dysplasia, hamartoma to benign neoplasia with occasional recurrence. Furthermore, once diagnosed the management of each is different. For cemento-ossifying dysplasia, this may mean doing nothing, simply because no treatment is generally appropriate. Almost all cemento-ossifying fibromas should be treated surgically, whereas cases of fibrous dysplasia are treated according to their clinical presentation, ranging from review and follow-up to surgery necessary to save the patient's sight or reduce deformity. The most important and frequent features of the FOLs differential diagnosis is discussed with assistance of a flow-chart.

Introduction

"The term fibro-osseous lesion (FOL) is a generic designation of a group of jaw disorders"[1] characterized by the replacement of bone by a benign connective tissue matrix. This matrix displays varying degrees of mineralization in the form of woven bone or of cementum-like round acellular intensely basophilic structures. The last are indistinguishable from "cementicles".[2]

The maxillofacial FOL considers lesions that are different (with the exception of fibrous dysplasia) to those found in the rest of the skeleton (see O'Hara[3] and Unni[4]). The term FOL in the maxillofacial region is applied to cemento-ossifying dysplasia (COD), fibrous dysplasia (FD) and cemento-ossifying fibroma (COF)[5] and their subtypes.

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The importance of radiology to the diagnosis of FOL

Maxillofacial FOLs are of particular interest to the radiologist because they emphasize the central role of the radiologist in the diagnostic process. This role arises because the pathology for all FOLs is identical, although they range widely in behaviour, from dysplasia, hamatoma to benign neoplasia with occasional recurrence. The late Charles Waldron wrote "In absence of good clinical and radiologic information a pathologist can only state that a given biopsy is consistent with a FOL. With adequate clinical and radiologic information most lesions can be assigned with reasonable certainty into one of several categories".[5] Conversely in the absence of such information Eisenberg and Eisenbud[6] stated that "pathologists today will often rightly decline to render a definitive diagnosis... Instead, the pathologist will resort to the noncommittal designation of *benign fibro-osseous lesions* [their italics]. This is the only acceptable approach considering the potential for inappropriate treatment otherwise." Therefore the identification of the majority of FOLs is made upon clinical and radiological features.

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Radiological assessment of the anatomical location of a bone tumour, its shape and size, the pattern of its matrix and its destruction, the definition of its margins and concomitant soft-tissue abnormalities generally correlate with its behaviour (aggressive or benign).[7] "Periosteal reaction" an important feature considered by skeletal radiologists "is not a feature of benign fibro-osseous lesions".[8]

Many FOLs, particularly COD,[5] are symptomless and require no surgery. Therefore diagnosis of the lesions on clinical and radiological features alone may obviate the need for an otherwise unnecessary invasive procedure. This avoidance of surgery could benefit the patient, because exaggerated growth of FD may be stimulated by surgery in young patients.[9]

The classification and nomenclature of FOLs

FOLs of the jaws have been subject to frequent renaming and reclassification; the development of this nomenclature and classification is summarized in Fig. 1.[5,10-23] Fig. 1 includes only those terms that appear to be still in use, and therefore, still clinically relevant. Nevertheless, this simplified figure is still able to display the "lumping" and "splitting" that appear to attend frequently the development of most classifications and systems of nomenclature. In the first edition of the WHO classification of "odontogenic tumours" (1971) four lesions containing cementum-like structures were identified.[10] These "cementomas" were the benign cementoblastoma and the cementifying fibroma, periapical cemental dysplasia and the gigantiform cementoma. They were placed within the "neoplasms and other tumours related to odontogenic apparatus" category. The other lesions that are frequently histologically indistinguishable from those four, FD and ossifying fibroma, were placed in the category of "neoplasms and other tumours related to bone". Since then a number of amendments to this classification have become necessary. The observation of identical cementum-like tissue in lesions in extra-gnathic sites suggested that this tissue may be a merely normal variant of bone;[24] and that dental cementum itself is a specialized form of "bundle-bone".[11] Therefore, in the second edition of the WHO's classification in 1992,[11] three of the "cemental" lesions were transferred to the "neoplasms and other tumours related to bone" group, leaving the benign cementoblastoma as the sole true neoplasm of dental cementum. A number of recent medical texts still refer to the first edition, such as that by Unni.[4]

Although the term FOL is not mentioned by the authors of WHO's second edition,[11] their broad reclassification of these lesions, based both on behaviour and histopathology, is entirely consistent with Waldron's recommendations made in 1985.[20] The FOLs are now a subset of "neoplasms and other tumours related to bone".

The radiology of FOLs affecting the face and jaws

Fibrous dysplasia (FD)

FD is an important lesion affecting the maxillofacial region because it can cause severe deformity and asymmetry, and most devastating of all, blindness. Although according to various authorities, including Waldron,[5] the majority of cases "burn out" in early adulthood when skeletal maturity has been reached, according to Eisenberg and Eisenbud[6] there are no studies of FD cases followed up over a long period to substantiate that view. Their contention is supported by later recurrence or reactivation in a small number of FD lesions followed over a long time, such as a report of two White cases,[25] and one of a Chinese case.[26] Other cases of FD have either been reactivated or first activated by pregnancy, suggesting that sex hormones could influence at least some of them. Furthermore, a number of cases continue growing into adulthood or first present clinically in adulthood.[27,28] Sakamoto and co-workers[27] report six of their 62 Japanese cases of FD presenting in the sixth and seventh decades. Garau and co-authors[28] reported that nine out their 12 cases of gnathic FD presented in Italians over 20 years of age; two in the seventh and eighth decades. It is possible that these reports may merely reflect the ages the lesions were first detected, diagnosed and recorded rather than a later age of commencement of growth. A late detection of a long-standing lesion is entirely possible because many cases of FD are painless.[26]

The range of behaviours suggests that the pathogenesis of FD may be complex. Chapurlat and Meunier[29] has proposed recently such a pathogenesis, which interrelates many of the salient features, elevated cAMP, increased expression of the proto-oncogene, c-fos, abnormally differentiated osteoblasts, formation of abnormal bone, increase in sex steroid receptors, increased interleukin-6 (target of diphosphanate treatment) and osteoclasts. Furthermore, the

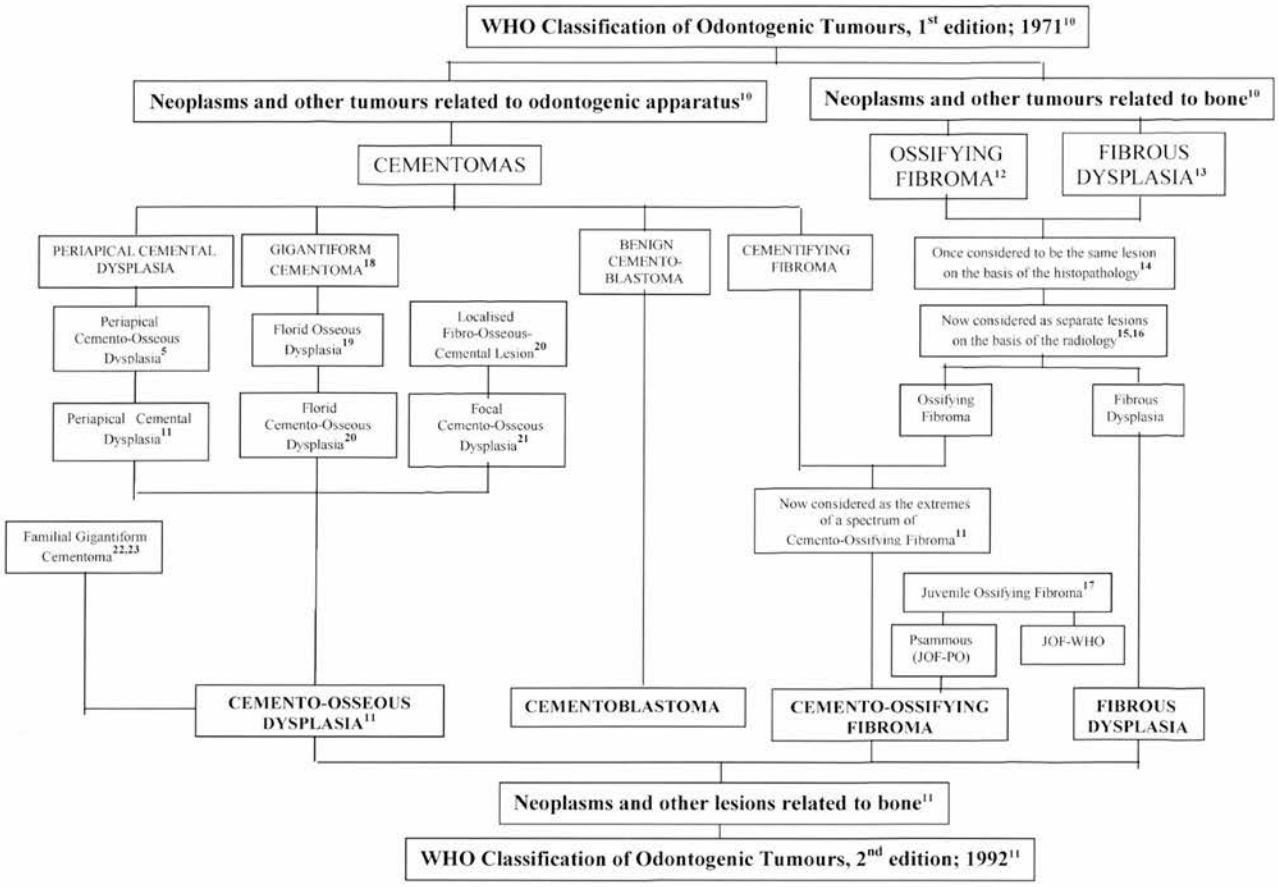

Figure 1 Summary of the recent development of the nomenclature and classification of fibro-osseous lesions of the jaws.

classical division of FD into monostotic, polyostotic and McCune-Albright forms may reflect the timing of the mutation, and thereby, the initial size of the mass of FD precursor cells.[30] The polyostotic form may arise in foetal life whereas the monostotic form may arise postnatally.[29,30] This correlates with the evidence that the monostotic form is not a precursor of the polyostotic form.[31]

The monostotic form accounts for 80-85% of cases of FD. Three percent of the polyostotic form have endocrinopathies[23] and are cases of McCune-Albright syndrome (precocious puberty and café-au-lait spots). McCune-Albright syndrome will not be considered further, because Fahmy and co-authors[32] have already fully discussed the radiology of precocious puberty and its extensive differential diagnosis. Although the term "monostotic" can be readily applied to cases of FD affecting the mandible alone, this is generally not so for FD affecting the maxilla or face. There FD can affect contiguous bones such as the zygoma and the sphenoid. These cases have been called "craniofacial FD".[23]

Polyostotic and McCune-Albright forms are easily diagnosed on clinical and radiological investigation alone. This is not so with the monostotic form, which has a number of other important lesions in its differential diagnosis requiring bone biopsy. Bone biopsy is generally avoided particularly where the risk of pathological fracture is high.[29] FD of the mandible differs in another important aspect from FD affecting long bones in that there does not appear to have been a report of pathological fracture of a dysplastic mandible.[26]

A radiological regime for polyostotic FD used by radiologists is scintigraphy and then plain film radiography of areas of increased radiolabelled uptake or activity. These films may be complimented by computed tomography (CT), which is especially useful for confirming the diagnosis and assessing the extent of the FD in the craniofacial skeleton.

The radiology of FD affecting the face and jaws gives an insight to its behaviour. Eversole's contention that in FD the teeth generally remain undisplaced with resorption, whereas COF may displace them or even resorb their roots,[33] is partly supported by a recent systematic review that found that over half of the teeth sited in dysplastic bone were undisplaced.[26] Furthermore, Petrikowski

and co-authors[34] suggested that "alteration of the lamina dura to the abnormal bone pattern, and narrowing of the periodontal ligament space are primary distinguishing features" for FD (Fig. 2). These phenomena in FD may reflect "programmed 'field effect' of abnormal osseous development in congenitally predisposed bone matrix".[6] This may account for the fusiform (spindle-shaped) expansion of FD of the affected bone (Fig. 3). In contrast, the displacement of teeth or resorption of their roots in COF represents the almost spherical centrifugal expansion that is associated with a benign tumour growing out from the probable site of origin (Fig. 4).

FD of the craniofacial complex may differ both radiologically and histologically from its counterparts in the axial skeleton. FD appears frequently in the latter as a circumscribed radiolucency with a thin sclerotic periphery, whereas cases of craniofacial FD, certainly those affecting the jaws and adjacent bones, are poorer defined and more radiopaque. A reason for the difference in appearance between maxillofacial FD and FD of the long bones is that the former occurs in skeleton derived from membrane bone.[33] The woven bone, which is well-mineralized, is arranged in a network of broad trabeculae. Furthermore, lamellar bone, generally absent in FD in the axial skeleton, occurs occasionally in FD of the face.[20,35] Particularly in the monostotic form, FD commonly displays an abnormal opacification, which ranges from the very numerous, small and diffusely distributed opacities ["ground glass" (Fig. 5) and "peau d'orange" (Fig. 2)] to sclerosis (Fig. 3), classically described as "cotton-wool". Different patterns may not only

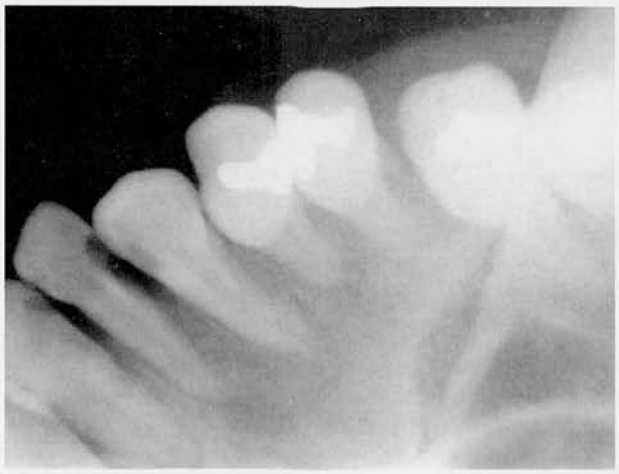

Figure 2 An oblique occlusal view of the hemi-maxilla, in a case of fibrous dysplasia (FD). The dysplastic bone presents with a peau d'orange appearance especially adjacent to the premolars. The lamina dura, which can be seen on the mesial aspect of the second incisor at the normal/dysplastic bone interface, is absent on the canine and premolars. The periodontal ligament space has been so reduced so as not to be visible around much of the canine and premolars. The buccal alveolar bone is expanded.

Figure 3 Part of a panoramic radiograph of a case of FD displaying fusiform expansion of the body of the mandible with downward displacement of the lower border and upward displacement of the alveolus. The dysplastic bone displays cotton-wool sclerosis. The normal/dysplastic bone interface is approximately sited in the middle of the ramus; the normal cortex delineating the normal follicle surrounding the crown of the unerupted third molar is only apparent distally, in normal bone. The inferior dental canal has been displaced downwards.

Figure 4 Part of a panoramic radiograph displaying an oval-shaped COF. It has slightly displaced adjacent teeth and displaced the inferior dental canal downward. It is well defined with a radiolucent space between the ground-glass opaque tissue and adjacent normal bone. Figure taken from Ref. 42 with permission.

Figure 5 An oblique occlusal view of the hemi-maxilla of a case of FD. The dysplastic bone presents with a ground-glass appearance especially adjacent to the molars. There is extensive expansion of the zygomatic bone; a very fine cortex is still visible.

be present in different parts of the same lesion, but may also depend on whether the film used is "direct exposure" or "fluorescent screen film".[20]

The margins of extra-gnathic FD appear well-defined, whereas they are poorly-defined in the jaws (Fig. 3). An objective definition of marginal definition has been described by Slootweg and Müller.[36] A lesion with a zone of transition less than 1 mm can be considered to be well-defined. This can be quickly and cheaply appreciated on plain film radiographs.

The expansion of FD of the mandible is classically spindle (or fusiform)-shaped when viewed on a true (axial) occlusal film (Fig. 6) or on a posterio-anterior projection of the mandible. The degree

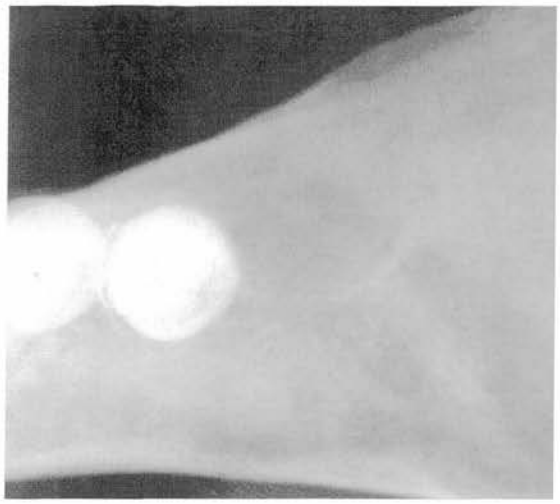

Figure 6 An axial (true) occlusal projection of FD affecting the edentulous posterior body of the mandible. It shows the typical fusiform expansion and gradual transition from normal cortex and trabeculae anterior to the dysplastic (ground glass) bone posteriorly.

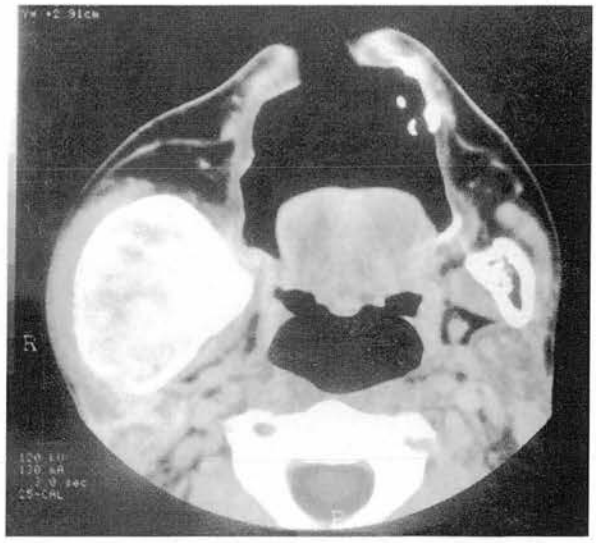

Figure 7 A soft-tissue window of an axial CT section of FD affecting the vertical ramus of the mandible. It expands the vertical ramus greatly in all directions; this expansion is remarkable on comparison to the normal contralateral side. This substantial expansion of the vertical ramus is accompanied by hyperplasia of the masseter muscle.

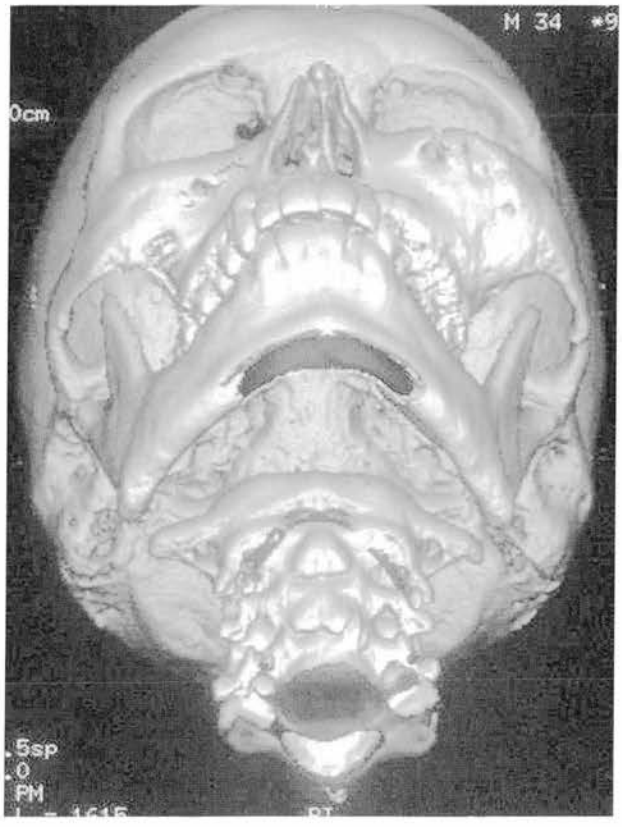

Figure 8 A three-dimensional reconstruction of a case of FD affecting the maxilla. The affected side though grotesque still adheres to the normal anatomical shape on comparison with the normal contralateral side.

of expansion can be remarkable, as apparent in Fig. 7. Although the shape of the FD affected maxilla appears to be more complex, reflecting the maxilla's complex structure, the overall effect is similar to that seen on the mandible. The expansion of the external surface of the affected bone assumes a more grotesque, but still recognizable shape (Fig. 8), whereas the internal surfaces expand into orbital, nasal and sinus cavities, fissures, fossae and neural and vascular canals. The lesion, if large, often nearly completely obliterates the maxillary sinus (Fig. 9). The above pattern is altered if the FD undergoes cystic degeneration with formation of a large aneurysmal bone cyst. Then the affected part of the lesion may lose its anatomical shape and becomes spherical (see figs. 2-4 of Ferretti and co-authors' report[37]).

If FD affects the orbital cavity or more particularly the optic canal, then blindness can result. Although the onset of blindness is generally gradual and may be intermittent, urgent surgery is frequently required to recover sight.[38] If specialized surgeons are not available then corticosteroids may help to alleviate optic nerve compression.[29,38]

Radiologists are familiar with an association of aneurysmal bone cysts (ABCs) and FD. Although the ABC is a well-recognized accompaniment to FD of the skull base it is not of FD of the jaws. Examples of the radiology of ABC secondary to FD of the mandible and of the maxilla are illustrated by Dorfman and Czerniak (their figs. 8-24[39]) and Lustig and co-authors (their fig. 2[31]), respectively. Another concern particularly in long-standing polyostotic FD is sarcomatous transformation, which can occur in absence of radiation therapy, 4% for patients with McCune-Albright, and 0.5% those with other FD forms.[40] Nevertheless, head and neck practitioners should be vigilant because the most frequent site for sarcomatous transformation is the craniofacial skeleton.[41] The features on conventional radiography that allow sarcoma to be differentiated from FD are permeative ill-defined borders, destroyed cortical outline and/or spiculated periosteal new bone formation and widening of the entire periodontal ligament space.[34]

CT has become an essential tool particularly for the investigation of the face and upper jaw, where the anatomy is not only complex, but because of the proximetry of the eyes and optic nerves. The CT images of FD will be discussed in relation to the CT images of COFs.

Figure 9 A bone window of a coronal CT section of FD affecting the maxilla. It obliterates almost completely the antral cavity. Although the lesion displays a generally homogenous ground glass appearance, there are areas that display both cotton wool and peau d'orange features. It extends into the hard palate, the alveolar process to envelop the molars' roots and the zygomatic arch (it has also secondarily envelopes the arch's medial surface). It displaces the inferior lateral wall of the nasal cavity medially. It also displaces the buccal (lateral) aspect of the maxilla laterally.

Cemento-ossifying fibroma (COF)

Ossifying fibroma and cementifying fibroma are now considered to be the two extremes of the same spectrum; because both frequently contain both bone and cementum-like tissue; these lesions are now called COFs.[11] The radiology of the COF in contrast to FD is well-defined and round or oval in shape (Fig. 4). In a recent synthesis 42, 34 and 24% were radiolucent, central radiopacity/ies and completely opaque.[42] Most COFs grow slowly, and once completely excised do not recur, but a minority, particularly in children (below 15 years of age[23]), exhibit rapid growth and a tendency to recur; the most frequent name applied to these lesions would appear to be "juvenile ossifying fibroma" (JOF).[17] Although this lesion is reasonably well-defined it may display erosion and invasion of adjacent bone (see Waldron's Figs. 14-60[23]). It is now clear that the term JOF has been applied to two quite different lesions. Slootweg and co-authors[47] first identified that the original WHO defined JOF (JOF-WHO), those affecting the jaws of children and presenting without cemental or psammomatoid tissue, are true JOFs, whereas those occurring in adults, mainly in sinonasal[17,33] and cranial bones,[33] and displaying cemental and/or psammomatoid tissue are actually COFs. Although Williams and co-authors[43] have suggested that JOF-WHO bears some histological resemblance to osteofibrous dysplasia, an extra-gnathic fibro-osseous lesion, they could not identify the cytokeratin-positive

cells of the latter in their JOF-WHO lesions. JOF occurs below 15 years of age, tends to recur, and is reasonably well-defined. Regardless of the eventual taxonomy of this lesion, like the COF it requires surgical treatment.

Another very rare, but important manifestation of COF is the multiple form. Hwang and co-authors[44] reported five rapidly growing separate COFs occurring in all four quadrants of the same patient over an 18-year-period. Multiple COFs occurring in the jaws may mimic polyostotic FD.[45]

Computed tomography (CT) and magnetic resonance imaging (MRI) of FD and COF

CT images of FD on bone windows can display the range of opacification observed on plain radiographs. CT of COF exhibits a thin intact cortex. Wenig and co-authors[8] have suggested that the cortex of COF on CT is thicker, but this feature has not been objectively evaluated.

Signal intensity on T1 and T2-weighted MRI images is dependent upon a number of factors such as the amount of bone trabeculae and degree of cellularity.[46] FD and COF both show intermediate signal on T1 and a hypointense signal on T2 weighting.[8] The hypointense signal intensity on T2-weighed images is caused by numerous bony trabeculae.[45] In the early stage of FD there may be areas of T2 hyperintensity.[8] This may correlate with the bone resorption phase of early FD. Although intravenous contrast medium (GD-DTPA) administration produces a moderately enhanced signal for COF, it is often marked for FD. Although both FD and COF can be mistaken for meningioma on MRI,[8] MRI offers greater specificity where there is neurovascular and ocular involvement.[38]

Three-dimensional bone reconstruction with helical CT allows optimal visualization of the extent of FD involving the skull base, particularly the optic canal,[47] which in turn allows the surgeon to choose the optimal approach for that particular patient. Three-dimensional reconstruction can further assist the surgeons in planning by computer-aided manufacture (CAM) model-making.[48] As most FDs affecting the face and jaws are largely unilateral a three-dimensional mirror-image of the normal contralateral orbit can made. This improves the likelihood of post-operative symmetry.[48]

In view of the continuous progression in some FDs Posnick[49] has advocated life-long continuous follow-up. He has also advised that post-operative CT is periodically needed "to confirm non-progression of any residual fibrous dysplasia".[50]

Cemento-ossifying dysplasia (COD)

Although there may be now little pathological[6] or radiological[51,52] rationale for the once purported periodontal origin for all or perhaps even most of these lesions, there is little doubt that CODs are linked in some way to the presence of teeth.[53] They are almost exclusively confined to the alveolar process; in the mandible they are found superior to the inferior dental canal (Figs 10 and 11). This confinement to the alveolar process strongly suggests an odontogenic origin.[53] Kawai and co-authors[51] observed six patterns of lesions. These lesions could be broadly divided into two main types: those that were clearly in contact with the root or hypercementosis and those that were separated from it by a radiolucent line that appeared to be continuous with the periodontal ligament space. They suggested the latter could have partly or wholly been derived from the medullary bone rather than from the periodontal ligament. Follow-up of some of these cases suggest that very few individual lesions change from one pattern to another, although new lesions may arise in previously normal sites. Inspection of their Table 3 revealed that the latter occurred among the youngest patients. This could suggest that in the majority of cases the condition developed on a lesion-by-lesion basis with increasing age until stability was achieved in old age. This would be consistent with the circumstantial evidence of such progression observed in another oriental report,[54] solitary lesions were observed in the young adult age group, and multiple lesions unilaterally distributed in the middle age group, and the bilateral bimaxillary lesions in the oldest age group.

The second edition of WHO classification in 1992 recognizes three separate COD entities, "periapical cemental dysplasia" (PCD) (Waldron referred to this lesion as "periapical COD" (PCOD)[5,23]), "florid COD" (FCOD) and "other COD".[11] The authors of the second edition recognized these categories "because it is useful to describe certain more or less well-defined clinicopathological presentations, without rejecting the possibility that they may be related to one another".[11] According to Waldron,[5] "they appear to represent only variants of the same disease process". PCD and FCOD display multiple lesions. The "other COD" category includes all those CODs "which share some features of PCD or FCOD, but do not have their characteristic clinicopathological patterns of presentation",[11] such as the focal COD (FocCOD), which is a solitary lesion.[21] Each separate or discrete lesion in all entities can display a similar range of presentations, ranging

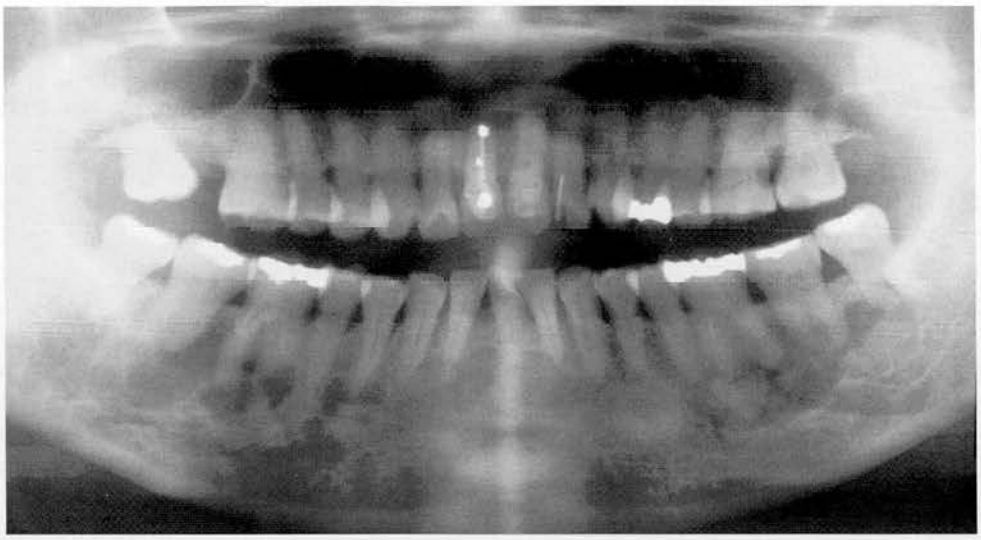

Figure 10 Panoramic radiograph showing the multiple lesions of FCOD. They present as radiolucencies associated with many mandibular teeth. Many of these radiolucencies contain one or more radiopacities. They are all superior to the inferior dental canal. The hard palate immediately adjacent to the alveolar process presents as two horizontal radiopaque lines. the upper line is the secondary image of that of the contralateral side.

from largely radiolucent (Fig. 10) through increasingly opaque to complete opacification (Fig. 11).[51] When the lower incisors (which are classically vital) are only involved it is commonly called PCD whereas when two or more quadrants are affected then it is frequently diagnosed as FCOD (Fig. 5). Classically the individual lesions of FCOD appears as lobulate masses, which may "attain a considerable size and cause expansion of the jaw", whereas those of PCD "rarely exceed 1 cm in diameter".[11] Even before the WHO second edition blurred the distinction between PCD and FCOD, by claiming PCD can occur in posterior sites, PCD was shown in a very recent systematic review (SR) to have been used as a synonym for FCOD in a number of reports.[55]

Although the nomenclature for FCOD is extensive, the older and more general terms were more effective in recalling SR-identified reports.[55] The term "gigantiform cementoma" once a frequent synonym, still occasionally used, would appear to have been used in the literature first by Gorlin and his co-authors in 1961.[18] Another old synonym, which still arises in connection with FCOD, is "chronic sclerosing osteomyelitis". Eisenberg and Eisenbud[6] have suggested that this last term should no longer be applied to FCOD, because "no one has demonstrated that the osteomyelitic process is

Figure 11 Panoramic radiograph displaying the multiple lesions of FCOD. They present a dense irregular radiopacites associated with most of the mandibular teeth. There are also some dense opacities in both edentulous maxillary quadrants. The defect in the alveolus in the lower left quadrant is occasioned by a recent extraction.

sclerosing". This of course does not exclude the possibility of chronic osteomyelitis occurring in a pre-existing FCOD.

The above SR[55] reported that 59% of cases occurred in Blacks, 37% in Orientals and 2% in Caucasians (including Indians); there was no difference in presentation between them. Cases in a report derived from pathology files,[54] as is most usual, appear to be older than those in a report based on radiology alone files.[56] Thus the generally reported older age of these lesions may reflect the fact that most remain symptom free and do not indicate the surgery necessary to produce the pathological specimen.[55]

Both FCOD and PCD are most prevalent in women of middle to old age, 92% in the SR on FCODs.[55] This would suggest that sex-linked factors are implicated in the aetiology. Furthermore, the mean age of the five male patients out of Kawai and co-authors[51] 54 CODs was 64.4 years compared with the females 49.4 years. This could suggest that female sex-linked factors do not only play a role in the high prevalence of this disorder among women, but also in the development of these lesions at a younger age than in males. Although the mean age in women is broadly coincident with the onset of menopause, the absence of a gynaecological history in all reports means that this association should be considered to be circumstantial.

Once the diagnosis has been made, no treatment is indicated; surgery and tooth extraction are used only when more conservative treatment has failed. This strategy minimizes the frequency of post-operative complications and poor tolerance of mucosal-borne dentures.

The third type of COD, the single or solitary lesion of the FocCOD is histologically indistinguishable from the individual lesions of FCOD and PCOD.[21] FocCOD like other CODs is more common in females. When Summerlin and Tomich's[21] White: Black 129:70 ratio is adjusted for the lower proportion of Blacks to Whites in their report (32%), there is a predisposition for Blacks (129:148), as seen in other CODs. FocCODs have been reported in the Chinese.[54] FocCOD can develop subsequently into PCOD and/or FCOD.[5,21] Unlike PCOD and FCOD, the radiological features of FocCOD are not sufficiently specific to differentiate them from small COFs.[23,57] Therefore "an absolute key....is the gross appearance at surgery".[53] When curetted FocCOD produces, with difficulty, only a few scraps of tissue, whereas COFs are more readily shelled-out, because they "are sharply demarcated, encapsulated with an edge clearly separate from surrounding bone".[53] Because of this difficulty in pre-surgical diagnosis, that may require surgery, FocCOD is perhaps the most common FOL in pathology files.[23]

Although COD has a predilection for those of African or Oriental origin,[29] a small number of Caucasian families display a clear autosomal dominant pattern.[22] Waldron called this form of COD "familial gigantiform cementoma" (FGC).[23] Both sexes are affected equally and FocCOD manifests at a younger age, perhaps as young as 4 years old.[22] Recently FGC has been reported in a 16-year-old Japanese boy, his father and grandfather.[58] Unlike conventional COD, FGC may undergo such extensive and even rapid expansion that surgery is required.[22] The Japanese boy experienced such florid growth of his lesions that over the 5 years after the initial diagnosis his lesions caused severe deformity of both jaws.[58] The behaviour can vary from one individual to another in such kindred, one displaying non-expansile lesions while others display substantial expansion.[22] The behaviour of the FGC can be so aggressive that it can, on occasion, be diagnosed as multiple COFs.[58] A family history may not always available or ascertainable.[59] A 20-year-old Chinese man presented with a 2-year history of progressive painless swelling of the mandible and pressure on the left eye. Radiographs showed that both jaws, including both antra, were completely filled with COD lesions, only the symphysis menti and ascending rami were spared. No family history was given.[60]

An important association of the COD is the traumatic (simple) bone cyst (TBC). This appears as a moderately defined radiolucency, which in a dentate area displays "scalloping", as its superior border (in mandibular TBCs) undulates around and between the roots, as is apparent in Fig. 10. Classically the TBC displays little or no bucco-lingual expansion, but those associated with COD frequently exhibit bucco-lingual expansion and displace the inferior dental canal downwards.[61] Furthermore, Melrose[53] noted that the classical TBC that affects teenage patients will generally heal completely after surgery, whereas those associated with FCODs may not do so. Instead they are filled in by abnormal mineralized tissue similar to that of COD.

Differential diagnosis of FOLs

The majority of lesions that appear prominently in the differential diagnosis of FODs are radiopacities occurring in the jaw bones; these are idiopathic osteosclerosis (IOS),[62] condensing osteitis (CO; secondary to dental inflammation),[62] and odontomas.[63] Once the film-development artefacts, and

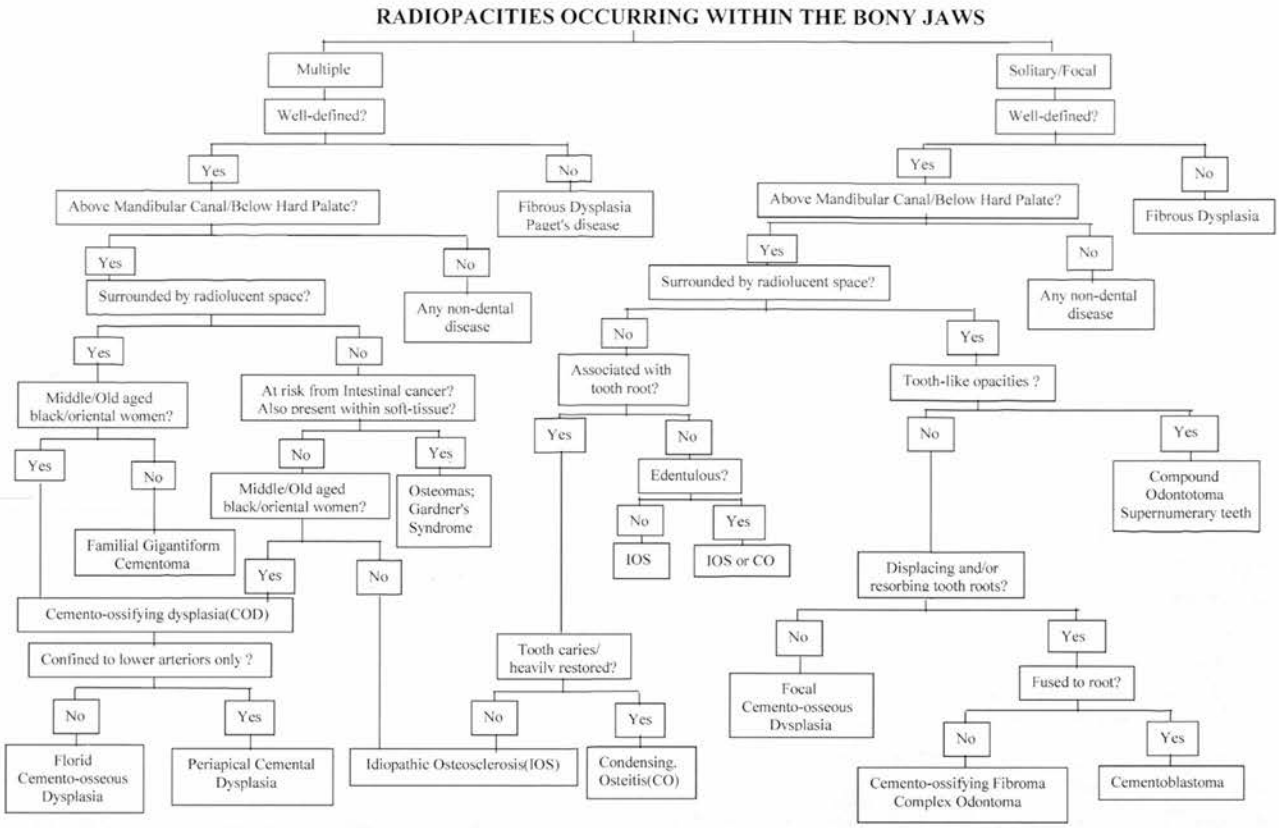

Figure 12 Radiopacities occurring within the bony jaws.

soft-tissue and metallic (iatrogenic) radiopacities have been excluded then four important aspects of the radiopacities can be considered sequentially as shown on the flow-chart (Fig. 12). These are:-

1. Are there multiple or single (solitary or focal) radiopacities?
2. Is the radiopacity/s well-defined?
3. Is the radiopacity/s sited above the mandibular canal?
4. Is the radiopacity/s surrounded by a radiolucent space?

Multiple or single lesions suggests differing aetiology, the former a likely systemic cause and the latter a local cause. It can be seen from the flow-chart (Fig. 12) that all of the multiple lesions have recognized familial (Gardner's syndrome, FCOD and PCD) and perhaps even a genetic tendency (FGC).

It is now generally accepted that it is reasonable to use the mandibular canal (inferior dental canal) as an arbitrary limit to the alveolar process or the tooth-bearing part of the jaws, particularly because the teeth develop above it in the foetal jaw and generally retain that relationship. Nevertheless, it should be noted that not only do lesions with a clear odontogenic origin, such as odontomas[63] (Figs 13 and 14) and cementoblastomas[64] (Fig. 15), arise within the alveolus, but so do others, such as CODs, IOS (Figs 16 and 17), and the majority of COFs, which do not appear to have a clear odontogenic origin. As they expand they will generally displace the mandibular canal downwards (Fig. 4). Conversely, lesions arising below it may be considered to be non-odontogenic lesions, which if sufficiently large may displace the mandibular canal upwards, as demonstrated of FD by Petrikowski and coauthors.[34] The subjective impression that lesions common to the general skeleton appear intrinsically to abhor the alveolus is false, as FD also on occasion displaces the mandibular canal downwards (Fig. 3), indicating that it may have initially arisen within the alveolus. A more likely reason is that the alveolus proportionally occupies such a small volume of the jaws with a proportionally smaller chance of general disease arising in it. It is also relatively transient; it can atrophy spectacularly after removal of the teeth.[65]

The maxilla does not have such a well-defined arbitrary limit for the alveolar process, because the superior alveolar (dental) nerve, the maxilla equivalent of the mandibular nerve, is not radiologically apparent. Nevertheless, an arbitrary margin for the superior margin is fairly easy to define.

Figure 13 A periapical radiograph showing a compound odontoma, consisting of several denticles (small teeth with a simple crown form), associated with an unerupted lateral incisor with an enlarged follicular space. Figure taken from Ref. 63 with permission.

Radiographically, on both panoramic radiographs and lateral cephalograms the alveolar process is below the image of the hard palate (Fig. 18). Any radiopacity confined to the alveolar process below the hard palate may be considered to be those lesions already mentioned with regards to the mandibular alveolus. Although the boundary between the maxillary antrum and the alveolus is very variable, with the antrum frequently pneumatizing the alveolus especially in the premolar region, the antrum's response to disease can assist the radiologist. Its obliteration by odontogenic tumours and FD differentiates them from Paget's disease, which generally spares the antral lumen. Benign neoplasms and odontogenic cysts displace upwardly the antral floor to create a rounded expansion when seen on panoramic radiographs and lateral views (Fig. 14). Their radiodensity readily allows their differentiation from lesions arising within the antral mucosa, such as the antral mucosal cysts (Fig. 18), which are obvious only by being silhouetted against the air-filled antral lumen.[66] It is also important to appreciate that

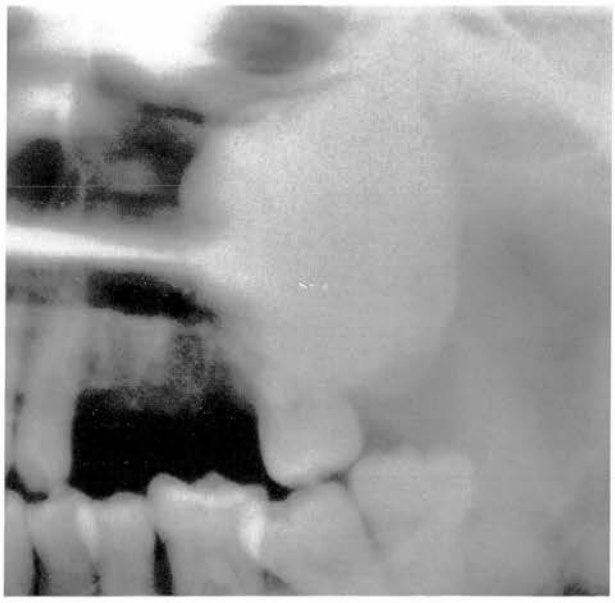

Figure 14 Part of a panoramic radiograph showing a large round complex odontoma occluding the posterior portion of the left maxillary antrum. It has expanded the posterior wall of the maxillary antrum. Figure taken from Ref. 63 with permission.

cystic lesions arising from odontogenic tissue, such as keratocysts, dentigerous cysts and unicystic ameloblastomas, can also similarly appear as radiopacities in the antrum, but, unless secondarily infected, can be distinquished from the MAC by having a radiopaque periphery representing the

Figure 15 Part of a panoramic radiograph of a cementoblastoma, which extensively resorbed the mesial root. The carious first premolar has a well-defined radiopacity at its apex, which should be considered to be CO rather than an IOS.

Figure 16 Part of a panoramic radiograph displaying a small very radiodense IOS at the apex of a non-carious tooth. It has a well-defined periphery.

Figure 17 Part of a panoramic radiograph displaying a large lightly radiodense IOS at the over the root of a non-carious tooth. It has a well-defined periphery.

upwardly displaced floor of the antrum (see MacDonald-Jankowski's figures for keratocysts[67]). Also unlike lesions arising within the alveolus the floor of the antrum below a MAC appears as an intact and undisplaced cortex.

Of course flow-charts cannot fully provide for all rare exceptions without becoming unduly cumbersome. Rare lesions such as multiple COFs are only occasionally reported in the literature, a testimony to their rarity. "Any other non-dental disease" refers to those radiopacities generating diseases found in the rest of the skeleton such as sclerosing osteomyelitis, osteoid osteitis and osteoblastoma in the differential diagnosis of solitary/focal radiopacities, and metastasis from carcinoma of the breast, thyroid and prostrate in that of multiple radiopacities.

The differential diagnosis generally ranks the lesions in order of their relative prevalence, taking account of the patient's age, sex, race, country of origin and anatomical location of the disease. In the jaws over 90% of CODs occur in women, predominantly Black or Oriental, over 30 years of age. Site predilection of FD is for the maxilla,[26] whereas that for cementoblastoma[64] is the first molar and premolar and that for the PCOD is the mandibular incisors.[10]

FCOD is usually limited to the alveolar process, whereas chronic diffuse sclerosing osteomyelitis is usually a single lesion limited to the body of the mandible on one side extending from the alveolus to the lower border and occasionally into the ramus.[68]

The odontoma is actually a hamartoma.[63] The complex form of this lesion (Fig. 14) can display all the radiological features of COF. Although the majority of odontomas do not exceed the dimensions of normal teeth, a number of very large odontomas, especially the complex form, have been reported (Fig. 14).[63]

A further radiopaque lesion that appears with even greater frequency is IOS.[62] It is important to recognize this generally conspicuous well-defined radiopacity because it merits no treatment. It can be distinguished from COFs, FD and odontomas because it has no radiolucent periphery[62] and even if large causes no expansion.[69] The main difference between IOS and condensing osteitis (CO) is that the

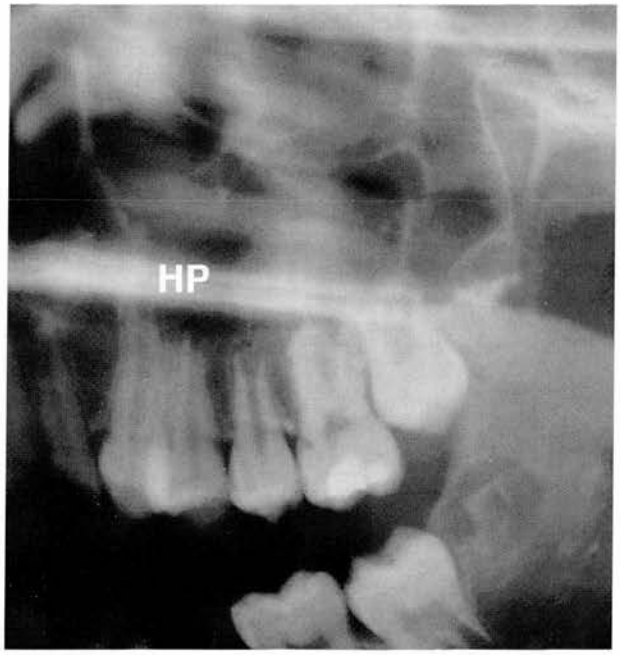

Figure 18 Part of a panoramic radiograph showing a mucosal antral cyst (MAC). Although a soft-tissue structure it is visible in the air-filled maxillary antrum by virtue of the "silhouette sign". It has no cortex and the corticated normal antral floor is intact and undisplaced. The hard palate immediately adjacent to the alveolar process presents as two horizontal radiopaque lines. The upper line is the secondary image of that of the contralateral side.

latter is directly associated with a carious or heavily restored tooth (Fig. 15) and is indicative of pulpal necrosis, whereas IOS may be associated with a non-carious or restored tooth (Figs. 16 and 17) or be completely unassociated with teeth, while still remaining within the alveolus. The radiodensity and size of IOS as with most other radiopacities observed can vary markedly (Figs. 16 and 17).

Conclusion

Diagnosis of a large FOL, although a technical challenge for the surgeon, is unlikely to challenge the specialist radiologist's or dental surgeon's diagnostic acumen as is clear in a recent report on FD.[26] Difficulty is more likely to arise with smaller lesions. For example a radiolucent lesion in an infant was diagnosed as a FD only to be diagnosed later as a JOF.[70] In another case a lesion labelled as an "atypical FOL" was subsequently found to be a low-grade osteosarcoma.[1]

The major problems encountered by the authors of WHO's second edition was not only the complexity of the tissues involved, but also the rarity of some lesions, which made it difficult to accumulate a large number for study and comparison.[11] Although the principles of systematic review have been applied to FD, the difficulty of this task has been aggravated by insufficient detail in the literature, particularly of radiological features.[26] A further difficulty is that, with the exception of a few long-term follow-up case reports, there are no reports of really long-term follow-up series of any FOL, in particular those that, on current evidence, do not merit surgery, such as FD and CODs.

The purpose of a clinical classification should be more than mere taxonomy, it should assist the clinician of the day to achieve a diagnosis that may be transformed into an appropriate treatment plan. With regards to COD, this may mean doing nothing, simply because no treatment is appropriate. Almost all COFs should be treated surgically, whereas FD cases are treated according to their clinical presentation, ranging from review and follow-up to surgery necessary to save the patient's sight or reduce deformity.

Although the present classification appears to have served us well for the moment, the deviant behaviour or presentation of a minority of lesions suggests that our understanding of these lesions is incomplete. Only further study with long-term follow-up of cases will confirm or refute this impression.

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